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BRITISH JOURNAL OF TUBERCULOSIS AND DISEASES OF THE CHEST

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THE EPIDEMIOLOGY AND EVOLUTION OF CHRONIC BRONCHITIS

BY C. H. STUART-HARRIS

From the University Department of Medicine, The Royal Hospital, Sheffield

THE awakening of interest in some half-forgotten neglected condition sometimes results from the development of a new method of diagnosis or treatment or because of a change in incidence, such as occurs in epidemic disease. But in the case of chronic bronchitis it is difficult to ascribe the present revival of interest to any one reason. Certainly the present trend of sickness in the ageing population of Britain emphasises the importance of chronic respiratory disease, both as a cause of ill-health and of mortality. Last winter's disastrous London fog also caused a greatly increased incidence of acute illness in chronically ill individuals and stressed the delicate balance of health in the chronic bronchitic subject. But neither in relation to diagnosis nor in treatment have substantial advances been made. Indeed, it is probable that recent successes in the treatment of tuberculosis may, by contrast, have made the problem of non-tuberculous respiratory disease appear more prominent, and have rendered urgent an attack upon the pathogenesis of chronic bronchitis and its attendant state of emphysema.

MORBIDITY DATA

To those familiar with the epidemiological method, our present inability to discern the pathogenesis of chronic bronchitis is hardly surprising. For the study of disease as a mass phenomenon can only begin when the subject under consideration has been defined, and the definition of chronic bronchitis is far from easy. Before, however, considering this, it will be as well to examine the present available data, which might be used in a consideration of the pathogenesis of bronchitis. Morbidity data have only been collected recently; they consist of sickness records from practitioners' attendances, industrial records and National Insurance data. A recent analysis of the National Insurance claims for sickness in 1950 (Digest of Incapacity Statistics, 1954) shows that something which is labelled bronchitis is of great importance. The six leading causes of sickness as judged by their frequency as a cause of spells of incapacity are shown (Table I) to be influenza, bronchitis, rheumatism (excluding rheumatic fever), pharyngitis and tonsillitis, common cold and gastritis. The incidence of gastric and duodenal ulcer and of pneumonia are shown in Table I

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NATIONAL INSURANCE

TABLE I.—SPELLS OF INCAPACITY FROM SICKNESS IN 1950 (GREAT BRITAIN)

	Males	*Females*	*Males*	*Females*
	Thousands		*Per cent.*	
All causes	4,458	2,246	100	100
Influenza	770	321	17·3	14·3
Bronchitis	421	169	9·4	7·5
Rheumatism	387	134	8·7	6·0
Pharyngitis, tonsillitis	235	198	5·2	8·9
Common cold	174	101	3·9	4·5
Gastritis	170	67	3·8	3·0
Gastric and duodenal ulcer	108	10	2·4	0·5
Pneumonia	26	6	0·6	0·3

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TABLE II.—CLAIMS OF SICKNESS 1950 (GREAT BRITAIN)

Age Distribution (per cent.)—Males

Condition	*All ages*	*Ages*					
		15–24	25–34	35–44	45–54	55–64	65 *and over*
Common cold ..	100	20	24	23	19	12	2
Pharyngitis, etc. ..	100	30	34	22	10	4	–
Influenza	100	15	23	25	22	14	1
Respiratory T.B. ..	100	21	28	21	18	11	1
Pneumonia ..	100	10	13	23	27	24	3
Bronchitis	100	7	13	18	27	31	4

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TABLE III.—CLAIMS OF SICKNESS 1950 (GREAT BRITAIN)

Age Distribution (per cent.)—Females

Condition	*All ages*	*Ages*				
		15–24	25–34	35–44	45–54	55 *and over*
Common cold	100	45	22	16	13	4
Pharyngitis, etc.	100	67	17	8	6	2
Influenza	100	39	20	17	17	7
Respiratory T.B.	100	55	28	10	5	2
Pneumonia	100	32	18	18	22	10
Bronchitis	100	30	17	18	22	13

for comparison. Now influenza, which in 1950 was not causative of an epidemic, is a term used diagnostically for illnesses at all ages, whereas pharyngitis and tonsillitis are much commoner in the younger than in the older groups of the insured population (Tables II and III). Bronchitis as a cause of sickness is scattered over the whole range of ages in women, but in men is clearly commoner

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TABLE IV.—DURATION OF INCAPACITY (MEN)

Condition	*Total spells (thousands)*	*Per cent. spells lasting more than*							*More than 100 days*
		6	12	18	24	48	72	96	
All causes	4,458	80	49	32	23	10	6	4	3
Influenza	770	75	35	16	7	1	–	–	–
Pharyngitis and tonsillitis, etc. ..	242	71	31	13	6	1	–	–	–
Common cold.. ..	174	67	28	11	5	–	–	–	–
Bronchitis	421	86	58	37	26	10	6	4	3
Pneumonia	26	99	95	86	78	40	18	8	5
Respiratory T.B. ..	20	98	94	91	88	80	74	68	63

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TABLE V.—DURATION OF INCAPACITY (WOMEN)

Condition	*Total spells (thousands)*	*Per cent. spells lasting more than*							*More than 100 days*
		6	12	18	24	48	72	96	
All causes	2,246	86	58	39	29	12	7	5	4
Influenza	321	85	43	21	11	2	–	–	–
Pharyngitis and tonsillitis, etc. ..	205	77	39	18	8	1	–	–	–
Common cold.. ..	101	75	34	14	8	2	1	–	–
Bronchitis	169	90	64	43	30	10	6	4	3
Pneumonia	6	99	95	87	79	42	22	11	7
Respiratory T.B. ..	9	99	96	94	92	86	82	79	75

in the older rather than the younger ranges. Naturally, as the available data give no clue to the number of insured persons in each age group from which the sicknesses are drawn, it is only possible to contrast the different diagnoses and the true age distribution of bronchitis cannot be deduced directly from the figures. Moreover the certification of an illness as bronchitis may mean either that the attack is one of acute bronchitis or that the illness is an exacerbation of

symptoms in chronically affected bronchitic subjects. There is no way of separating these two types of illness but some additional information is given by the duration of the illness. Tables IV and V give the duration of incapacity in the various spells of respiratory diseases already mentioned in Tables II and III. Both in men and women the duration of bronchitis is often protracted. Indeed, nearly 40 per cent. of attacks in men and over 40 per cent. in women last more than eighteen days, and 10 per cent. of attacks in both sexes last more than forty-eight days. As this latter figure means that more than 40,000 attacks of bronchitis in men last for more than seven weeks, the toll of the nation's economic life attributable to this form of sickness is heavy. There is also a sharp contrast with attacks of influenza or of pharyngitis which are mostly over in eighteen days. This suggests that doctors use the term bronchitis both for acute attacks, perhaps in previously healthy individuals, and also for the exacerbations of illness in patients with chronic bronchitis. It is also obvious that death certificates which mention bronchitis as a primary cause of death cannot be assumed to be records of deaths of patients with chronic bronchitis. Some 30 to 40 per cent. of all deaths attributed to bronchitis on death certificates have also had a secondary or contributory cause in the form of myocardial disease, and this could mean that the patient had coexisting hypertensive or coronary heart disease or that the condition of cor pulmonale was present. It seems unwise in the state of present knowledge to draw on mortality figures until more facts are known concerning morbidity.

Chronic Bronchitis in General Practice

Most clinicians would agree that the clinical characters of an established state of chronic bronchitis with superadded emphysema are cough, expectoration and breathlessness. These symptoms are, however, encountered in many other conditions and, without further investigation, the delineation of chronic bronchitis is extremely difficult. Even so, this has been attempted and Fry (1954) has analysed 127 cases in his own practice and has graded them in terms of severity into four groups. The mildest form was a state of a recurrent winter cough, usually following a cold, then came those patients with acute exacerbations in winter time, next those with symptoms all the year round and, finally, those rendered totally invalid. In view of the long duration of the state of chronic bronchitis it must be obvious that the delineation of the earliest stages must be more difficult than of the later phases when symptoms are persistent.

In 1951 a field survey was carried out by the staff of my Department which altered the perspective of our group. 406 male volunteers from a mixed industrial undertaking were examined clinically, radiologically and by vital capacity and maximum breathing capacity tests. Volunteers with symptoms and those who considered themselves healthy were examined and three categories of men were separated. An abnormal group of 90 men consisted of those with established disease of the heart or lungs or both. A healthy group of 81 men, aged 30 or more, who were the fittest in these ages, was also distinguished. The remaining 235 men included many who were well but also a minority with abnormalities of a clinical or radiological or functional character

who could not be classified accurately. The accompanying Tables VI–VIII indicate the results of the survey in terms of symptoms and more accurate diagnoses. Tables VI and VII indicate the incidence of cough and sputum (excepting those with an intermittent sputum only experienced during colds) and also a third symptomatic group called the " Triple Complex." This was the syndrome of cough, sputum and disability. The latter consisted of a complaint of habitual or winter attacks of " bronchitis " or else of dyspnœa of a certain grade (on walking, or on stairs, or any degree of exertional dyspnœa which had been present for three or more years). The purpose of the " triple complex" was

TABLE VI.—ANALYSIS OF SYMPTOMS OF BRONCHITIS IN AN INDUSTRIAL POPULATION

Whole population	*Numbers*	*Cough and sputum*	*Per cent. of total*	*" Triple complex "*	*Per cent T.C. of total*
Under 30 years	112	22	19·6	1	0·9
30–39 years	112	44	39·2	12	10·7
40–49 years	91	33	36·2	20	21·9
50–59 years	65	36	55·3	23	35·5
60 years and over	26	15	57·6	11	42·3
Total	406	150	36·9	67	17·2
30 years and over	294	128	43·5	66	22·4

TABLE VII.—INCIDENCE OF SYMPTOMS IN ARTIFICIALLY SEGREGATED GROUPS

Categories	*Numbers*	*Cough and sputum*		*" Triple complex "*		*Clinical Bronchitis*	
		Number	*Per cent.*	*Number*	*Per cent.*	*Number*	*Per cent.*
Abnormal	90	70	77·7	48	53·4	53	58·8
Healthiest over 30 ..	81	22	27·1	2	2·5	0	0
Intermediate	235	58	24·7	17	7·2	14	5·9
Total	406	150	36·9	67	17·2	67	17·2
Hospital patients " Chronic bronchitis "	97	91	93·8	86	88·7	97	100

to attempt to define a symptomatic index found in a high percentage of subjects with proven chronic non-tuberculous chest disease, such as the group of hospital patients listed in Table VII. Table VI shows the increase in incidence of symptoms with age, the " triple complex " rising more steeply than cough and sputum alone. Table VII gives figures for the three artificially segregated groups of men in the field survey and mentions under clinical bronchitis those considered clinically to have the state of chronic bronchitis and emphysema but who had no other discoverable cause of their symptoms. Table VIII is a detailed analysis of the clinical findings in the group of 90 abnormal men and lists separately those with hypertension with or without cardiac enlargement,

pneumoconiosis and so on. It should be clear from this that it is extremely difficult even with such detailed examinations to draw sharp diagnostic lines. Many of the hypertensive patients had diminished ventilatory function of the lungs, some grossly so. Trivial grades of pneumoconiosis were sometimes associated with a considerable degree of cough and expectoration and the group of cases remaining in the category of chronic bronchitis included a few patients with bronchiectasis. The difficulty of attempting to define chronic bronchitis by the simple process of excluding all individuals with other conditions is evident.

TABLE VIII.—CLINICAL FINDINGS IN 90 ABNORMAL MEN

Diagnosis	*Numbers*	*Numbers with per cent. predicted pulmonary function*			*Cough and sputum*	*Clinical bronchitis*
		80 *per cent. or less*	70 *per cent. or less*	60 *per cent. or less*		
Hypertension						
With cardiac enlargement	13	7	7	3	11	0
Without cardiac enlargement	14	10	7	5	11	11
Pneumoconiosis						
Radiologically definite	9*	3	1	0	6	0
Radiologically trivial ..	6†	3	3	2	6	4
Miscellaneous						
Asthma	4	3	2	2	2	2
Unexplained cardiomegaly	3	2	1	1	1	2
Coronary heart ..	1	?	?	?	1	0
Rheumatic heart ..	1	0	0	0	1	0
Post-lobectomy (bronchiectasis) ..	1	1	1	1	1	0
Pulmonary T.B. (inactive)	1	•	0	0	1	0
Chronic bronchitis ..	43	28	20	11	35	35
Totals ..	90	55	40	24	70	53

* 3 noted also under hypertension with cardiac enlargement.
† 3 listed also under hypertension, 2 with and 1 without cardiac enlargement.
Pulmonary function assessed by vital capacity and maximum breathing capacity tests.

CHRONIC BRONCHITIS IN HOSPITAL

All patients attending hospital are selected in some way, and in the case of chronic bronchitis the process of selection is affected by the very long duration of the disease. In general two varieties of patients are seen, those with acute exacerbations of symptoms, and those with terminal states such as acute bronchiolitis or pneumonia or congestive heart failure. Other patients may be sent to the out-patient department for investigation of symptoms such as blood-streaking of the sputum, when a carcinoma is suspected, or because a specific

occupational cause is suspected. In spite of the difficulty in building up a picture of the natural history of the disease from so many different individual illnesses, a measure of agreement concerning the process exists between different observers. This is particularly the case for the advanced stages when recurrent breakdown of health results in inability to carry on with a previous occupation. This usually means that an advanced state of emphysema has developed which leads progressively into one of the two terminating phases of pulmonary insufficiency or chronic cor pulmonale. Both these phases of chronic ill-health are punctuated by periodical acute exacerbations when the obvious evidences of bronchial infection with purulent sputum and increased dyspnœa suggest that further damage to bronchioles and possibly also to the pulmonary circulation are in progress. Both the acute breakdowns in patients with bronchitis and those with cor pulmonale occur seasonally during the winter and are particularly numerous when winter epidemics of the respiratory tract (influenza and the common cold) are in progress.

In Sheffield, a rather large percentage of men who are admitted to hospital exhibits the state of chronic congestive heart failure, and some idea of the size of the problem has been obtained by Flint (1954) working at the City General Hospital. In a detailed analysis of the varieties of underlying heart disease in patients admitted to the hospital with congestive heart failure during a twelve-month period, Flint found that 64 of 159 male patients (40 per cent.) had chronic cor pulmonale, compared with 33 cases of coronary heart disease, 26 of hypertension and 26 of rheumatic heart disease. Among 141 females, there were 37 with hypertension, 32 with coronary heart disease, 42 with rheumatic disease and only 12 (8·5 per cent.) with cor pulmonale. In my own series of patients with cor pulmonale there have been even fewer females, the sex ratio among 64 patients being nine to one in favour of males, but Flint's series included a greater number of patients dying acutely following admission. Lest it be concluded that the sex incidence of cor pulmonale is due to the effect of specific occupational cause in the male, it is necessary to indicate the infrequency of pneumoconiosis in cases of this disorder in Sheffield. Flint found little evidence of pneumoconiosis in 5 of his 64 male patients, and I have personal experience of the concurrence of pneumoconiosis and cor pulmonale apart from a few men with minor radiological changes who also had severe emphysema. The majority of patients with cor pulmonale exhibit merely chronic bronchitis or bronchiectasis with accompanying emphysema such as is certainly also seen in women, though less often than in men.

In the case of chronic bronchitis unaccompanied by heart failure the sex ratio is four or five to one in favour of males, and this holds good not only for Sheffield but also for the large series of 1,000 patients studied at the Brompton Hospital by Oswald *et al.* (1953). The age distribution of the latters' patients is shown in Table IX, where the figures for sickness certificates from bronchitis taken from the National Insurance statistics are also shown. It is clear that the breakdown in health due to chronic bronchitis increases over the age of 40 and that the peak is in the sixth decade in male patients in both series. The correlation between age and incidence of attacks of bronchitis is indeed a striking finding, the age of onset of symptoms being more variable though generally placed ten or more years before health is seriously disturbed.

In regard to the other characteristics of patients with chronic bronchitis compared with those not so afflicted, it is as yet hard to find data which give a clue to pathogenesis. Oswald *et al.* (1953) stress the family history of bronchitis in near relatives, which is three times as common in bronchitic subjects as in other patients. This could, however, be explicable also on the basis of family infection rather than by genetic factors, and the occurrence of bronchitis in childhood is a well-known feature of the past history of some adult patients. The data concerning environment, occupation and climatic factors do not exist in a form which enables an assessment to be made concerning their causative influence. Pemberton (1952) and Goodman *et al.* (1953) have both analysed mortality statistics relating to bronchitis and have emphasised the sex difference, the greater incidence in the lowest social classes, the tendency to involve those working in dusty trades, and the unfavourable statistics from northern industrial areas. But no clear-cut etiological factor has been incriminated. There is little doubt that once chronic bronchitis has developed, occupa-

TABLE IX.—AGE DISTRIBUTION OF BRONCHITIS

	Sex	*Per cent. of affected individuals in various ages*					
		20–29	30–39	40–49	50–59	60–69	70 *and over*
Brompton Hospital* out-patients	Male	3·4	7·3	16·4	43·0	26·8	3·0
National Insurance Claims (1950)		11·0	14·0	22·0	31·0	60 *and over* 19·0	
Brompton Hospital* out-patients	Female	12·2	19·0	29·4	26·1	11·7	1·7
National Insurance claims (1950)		27·0	17·0	20·0	22·0	60 *and over* 2·0	

* Based on the figures of Oswald *et al.*, 1953.

tions involving heavy work in a smoky or dusty environment are harmful and so also is foggy weather. There is a need for much wider surveys than any yet made before the critical importance of specific environmental factors can be discerned. In such surveys a major difficulty is bound to arise in the delineation of early stages of chronic bronchitis, as has already been emphasised by the field work in Sheffield.

THE RELATIONSHIP BETWEEN INFECTION AND CHRONIC BRONCHITIS

There is little doubt that acute bronchitis occurs in previously healthy individuals as a result of infection of the respiratory tract. Children may develop bronchitis during a common cold or an attack of measles or whooping-cough. Servicemen without previous history of chest disease may develop acute bronchitis during influenza or the common febrile catarrh (acute respiratory disease of American authors). The unknown virus infection associated with atypical pneumonia is believed to cause attacks of bronchitis without discoverable radiological changes. All these instances of bronchitis in young adults are

probably virus infections in which the bronchi and the bronchioles are involved as part of the attack on the epithelium of the respiratory tract. They do not commonly, however, lead to any persistent chronic disease of the bronchial tract.

There is no doubt that similar attacks of acute bronchitis occur during the early life of individuals who later become crippled by chronic bronchitis, and it is difficult then to avoid an impression of cause and effect. The major difference between middle-aged healthy individuals and those with chronic bronchitis, however, appears to be the frequency of acute illnesses, some apparently precipitated by colds or attacks of influenza, and others by circumstances of a more remote character such as fog, exposure to dust and possibly even exceptional exertion. Even in attacks due to the latter causes, however, the evidences of an infective process can be found in the persistent presence of pathogenic organisms and particularly of pneumococci and *Hæmophilus influenzæ* in the sputum (Stuart-Harris *et al.*, 1953). It is still impossible to state whether such organisms are the cause of, or are the consequence of, the disordered state of the bronchial and bronchiolar tree. This has recently been discussed by Oswald (1954), who is inclined to blame an abnormal secretion of mucus by the bronchial epithelium for setting up a mechanical state favouring the development of emphysema and of persistent bacterial infection. The author's view is that the abnormal quantity of mucus secreted by the epithelium is the result rather than the cause of the infection. The presence of anatomical damage such as exists in cases of bronchiectasis and development of irregularities in calibre of bronchioles with areas of bronchiolar dilatation, such as have been found by Reid (1954) in cases of chronic bronchitis, must hamper the disposal of bacteria. Successive acute virus infections aggravate these local conditions and assist in chronic colonisation of the bronchial and bronchiolar tree, and spread of bacteria from affected to unaffected segments. The normal resistance of the bronchial tree to the presence of organisms is thus lost, and even if the epithelium remains intact, penetration deeply of species such as *Hæmophilus influenzæ* can occur, as has been demonstrated by Hers and Mulder (1953). The resultant state resembles that of a chronic wound infection which is kept in existence by intermittent traumatisation of the wound.

The Development of Emphysema

Although there is no doubt that hypertrophic emphysema sometimes arises as a result of other conditions such as asthma, the state of chronic bronchitis is much the commonest predisposing condition. The reason for the formation of emphysematous air-spaces is still far from clear, but partial blocking of the bronchioles would appear to afford the necessary mechanical resistance to airflow which leads to air-trapping. Mucus secretion, formation of a catarrhal exudate and swelling of the mucosal lining all occur in the bronchioles as a result of infection, and perhaps contraction of bronchiolar muscle may also be a factor in opposing the normal flow of air in and out of the alveoli (Fry *et al.*, 1954). It seems probable that emphysema develops patchily during acute exacerbations of infection in the bronchitic subject, but it is not at all clear when the event occurs in relation to the natural history of chronic bronchitis.

Once emphysema has developed, the stage is set for progressive disturbance of alveolar ventilation, and this may be an underlying factor not only in relation to dyspnœa but in the physiological upset which causes cor pulmonale. Perhaps the state of emphysema is more likely to occur in those subject to recurrent attacks of bronchitis under the influence of adverse environmental conditions, including severe exertion such as would be more likely to be experienced by men than women. It is, of course, a pure supposition in the present state of knowledge that it is the factor of emphysema developing secondarily to bronchitis which explains the age and sex incidence of the latter, and it is conceivable that genetic or hormonal factors may yet prove to be the missing epidemiological circumstance. But it is certain that infection alone cannot explain the variation in observed incidence of bronchitis, whereas infection plus a mechanical disturbance such as emphysema might be the answer.

Summary

Morbidity data referring to bronchitis in Great Britain are given and discussed. Bronchitis is used as a label for certification purposes both for acute illnesses in previously healthy persons and for exacerbation of symptoms in chronic bronchitic subjects. The data from general practice are confused by the simultaneous presence of hypertension or of pneumoconiosis or other diseases of the heart and lungs, and delineation of the early stages of chronic bronchitis is extremely difficult. Hospital experience underlines the importance of age in relation to breakdowns of a serious character and also the influence of the winter season. The significance of infection and emphysema in relation to the problem is discussed.

I am indebted to the Ministry of Pensions and National Insurance for permission to use their Digest of Incapacity Statistics in the preparation of the above paper. Research work on bronchitis referred to above is supported by a grant from the Board of Governors of the United Sheffield Hospitals.

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RECENT ADVANCES IN RADIOLOGY OF THE CHEST

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In the past few years great strides have been made in radiological technology. In most instances these new developments have found wide application, particularly in radiology of the heart and lungs. In fact, it is probably true to say that without these new advances little progress would have been made in diagnostic radiology.

It is not within the scope of this communication to discuss in detail all the new methods which have been developed, some of which are so highly specialised that they will only be mentioned in passing. It is, however, well worth while spending some time on the more important advances and viewing in perspective their impact on the radiology of the thorax.

A. Electro-technical Developments

1. High kilovoltage radiography.
2. Screen image intensification and magnification technique.
3. Electro-kymography.
4. Mass miniature radiography.
5. Multiple section and horizontal section tomography.

B. Methods for Standardisation of Technique

1. The photo-timer.
2. Automatic dark room processing.

C. Contrast Media

1. Bronchography with water-soluble contrast media.
2. Angiocardiography of heart, mediastinum and lungs.

A. Electro-Technical Developments

1. *High Kilovoltage Radiography and Image Magnification*

It is now possible with modern X-ray equipment to increase the peak kilovoltages up to 140. With the introduction of a high kilovoltage range and its application to chest radiography, one can reduce exposure time to insignificant fractions of seconds and thus lower the disturbing factor of movement. Another additional advantage of the high kilovoltage technique lies in a decrease in the incident X-radiation to the patient.

From the purely qualitative point of view, chest films taken at high kilovoltages appear rather grey and are not very contrasty, but the demonstration of fine lung detail, definition and shadow gradation is very much superior to that seen on films taken at standard kilovoltages which are in use at present. With this improvement in definition and finer gradation in contrast, direct-

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image magnification has become a possibility. This can be done quite simply by increasing the film tube distance to 12 feet and by increasing the patient film distance; it is, of course, necessary to use a high kilovoltage in the neighbourhood of 140 kV. and an X-ray tube which will not only be rated for this high kilovoltage but which also incorporates a very fine focus. The magnified image of a segment of lung will be of great help in elucidating small and doubtful opacities or shadows which are so tiny that their definition on standard radiographs is uncertain. This can be applied particularly to miliary opacities or in the investigation of the early stages of pneumoconiosis.

2. *Screen Image Intensification*

This new method was originally developed in the United States and a number of papers relating to the experimental work have appeared in the past few years in the literature (1951, Morgan and Sturm). The Westinghouse Corporation of America and Messrs. Phillips of Holland have been able to develop commercial units capable of intensifying the screen image, which can now be incorporated in existing standard radiographic units. These units are capable of intensifying the fluorescent screen image up to 1,000-fold without loss of definition or sharpness.

Two main systems have been developed, both of which give comparable results. In the one, direct viewing of the screen image is possible, and in the other, the screen has to be viewed through magnifying eyepieces. With this advance in X-ray fluorography it will be possible to screen in daylight with the obvious advantage of eliminating dark adaptation, and both radiologist and patient will enjoy unrestricted freedom in a brightly lit examination room. The incident X-radiation to the patient will be reduced to insignificant fractions, thereby greatly diminishing the danger of over-screening. The electric currents required for screening and film taking are very much smaller than those hitherto used, which will prolong tube life and make it unnecessary for generating plant to be provided with a very high output. By increasing the image brightness to such tremendous levels, shadows which might have been missed on fluorescent screens now in use will become quite obvious. The screen intensifier can be so adapted as to take either single 35-mm. films with an ordinary photographic camera, or a cine film with standard equipment.

This new method is, at present, only in its developmental stage. It is as yet too early to predict how far it will influence routine chest radiology. It is, however, quite obvious when one considers the points already mentioned that our standard techniques now in use will be greatly changed in years to come, particularly when this new apparatus has been further developed and becomes generally available.

One restricting factor at the present is the image size; this is relatively small in commercially available equipment and restricted in one apparatus to a circle of 6 inches, but no doubt within a short time larger images up to 14 inches should be available.

3. *Mass Miniature Radiography*

As a method, this is not a newcomer to chest radiography. There have, however, been some new technical developments of some significance. The

35 mm. film has been largely replaced by the 70 mm. film. Considerable progress has been made in the efficiency of modern photo-fluorographic cameras, and one need only mention the Schonander and Odelka mirror units. Definition on the 70-mm. film is of such good quality that only minor mangification is necessary, particularly if the films are only used for scanning purposes, which, after all, is the main function of mass miniature radiography.

If, on the other hand, a truly diagnostic radiograph is required, which is not of standard size, the 4 by 5 mm. camera is the one of choice. This film size is sufficiently large to make magnification unnecessary.

With recent trends in the extension of mass surveys, it is obvious that by using miniature films the saving in film expense is a considerable factor, quite apart from the essential value of these units in making a rapid and constant chest survey service possible. With the introduction of these easily handled, smaller and more efficient mass miniature units in the X-ray departments of general hospitals the mass chest surveys of the attending hospital population has been further extended, which will be of great benefit to the Tuberculosis Service in this country as a whole. It should be the aim of all X-ray departments in major hospitals to develop the mass miniature unit, so as to cover the entire attending hospital population.

4. *Tomography*

Although the method of tomography is now well established and has been in general use for many years, some important advances have been made in specialised apparatus which is now generally available. It is an established fact that tomography carried out with standard equipment which is used for many other radiographic purposes cannot give as good and constant results as a unit specially designed and used only for tomography. Most modern, specially designed apparatus now incorporates a fluoroscope, which makes positioning of the patient and an estimation of the depth at which the lesion is to be examined much simpler and more accurate. The patient can be radiographed in all planes, which is particularly useful if cavities or fluid levels are present. All movements of the tomogram are carried out automatically at constant speed and with accurate timing, both factors of great importance.

One other new advance which is not yet universally used is horizontal section tomography. This was originally described by Watson in 1939 and further developed by Stephenson in 1950. With this technique it is possible to take horizontal sections at any given level of the body, a useful additional method to localise accurately intrathoracic lesions in three planes. Multi-section planigraphy is yet another newcomer (1939, Watson; 1953, Watson; 1950, Stephenson).

With this device a large number of films can be exposed simultaneously, each individual film representing a section of the body at a different level. By using this type of tomography, over-irradiation of the patient will be avoided and X-ray tube life prolonged. The only disadvantage is a slight increase in the object film distance which will mean magnification of some of the shadows cast, but in most instances this is not a disturbing factor.

B. Methods for Standardisation of Technique

1. *The Photo-timer*

With this instrument it is possible to standardise radiography and make exposures independent of line voltage fluctuations and personal variations in judging radiographic factors. This is particularly important when chest radiographs are required for comparison or follow-up studies, quite apart from the great advantage of obtaining standard radiographs of good quality.

A number of these instruments are commercially available. The best results will be obtained with apparatus which will scan a large area of the chest and not only a small segment of the lung or mediastinum (1948, Bischoff; 1953, Clarke). If used in conjunction with mass miniature units, not only will there be an improvement in the quality of the film, but the time-saving in X-raying a large number of patients will be significant.

2. *Automatic Dark-room Processing*

No matter how reliable and accurate the radiographic technique, the final effect will depend on the dark room. Although in most centres standardised dark-room techniques have been instituted, the results still fall very short of perfection, owing to inconsistencies in the composition of processing solutions, developing temperature and processing time, and the personal factor of the technician. To overcome these difficulties automatic processing units have been developed. The films are carried through the various stages of processing by a conveyor-belt system. These units are now sufficiently reliable to ensure standard developing time and temperature, as well as a standard concentration of the solutions, and, provided that the radiographic technique is adequate, the final results should be perfect (1951, Hills).

C. Contrast Media

1. *Water-soluble Substances for Bronchography*

These were first developed in Sweden in 1950 and many papers have appeared in the literature relating to their use (1951, Nordenstrom, Norlin; 1951, Charpin, Metras, Gaillard; 1952, Conway).

The great advantage of these drugs lies in their absorbability and subsequent excretion by the kidneys, thus clearing from the lung within hours or days after the examination. Alveolar filling of the lung with these new materials is less marked and slower than with lipiodol, which makes it less necessary to speed up radiography, and this in turn helps to position the patient adequately.

These new subtances have only been introduced into this country within the past years, but they have already replaced lipiodol as the routine bronchographic medium in many centres. They are slightly more irritating to the bronchial mucosa than lipiodol, but provided that preliminary anæsthesia is adequate, the bronchographic technique is in no way more difficult than with lipiodol or allied substances. Xylocane, 2–4 per cent. is probably the most useful surface anæsthetic to use. Any one method can be used to instil the contrast medium into the bronchus if it is carried out skilfully, and under satisfactory conditions no specialised techniques are needed to obtain adequate results for diagnostic purposes.

2. *Angiocardiography and Pulmonary Angiography*

These are now well-established methods of investigation of cardiac pathology, particularly of congenital heart disease, lesions of the mediastinum and great vessels in the chest. These methods will rarely be employed for the investigation of pulmonary lesions, with the exception of arterio-venous fistulæ or vascular tumours. The results have been widely published in the literature during the past few years and a variety of techniques and specialised apparatus for rapid cassette changing have been developed (1951, Dotter, Steinberg; 1953, Goodwin, Steiner, Mounsey, MacGregor, and Wayne).

It cannot be too strongly emphasised that angiocardiography should not be used indiscriminately. The method should only be reserved for those patients where there are definite indications, such as a pre-operative measure, or where other more simple technical procedures have failed to establish the diagnosis. The procedure should not be carried out in centres where there is not a fully trained team available, conversant with the various clinical and technical aspects of angiocardiography. It is, after all, a highly complex procedure which carries definite risks, and these must be weighed very carefully against any possible value accruing from the examination.

Conclusion

A variety of technological advances have been described and their application, particularly to radiology of the chest, has been discussed.

It is impossible to predict what the future holds, but there can be little doubt that with these new developments great strides have been made and further benefit will be derived from them in the future, once they have become well established as routine procedures.

It appears at present that X-ray technology has advanced well ahead of clinical developments. Only time will close this gap and, if one may speculate on future trends, it is very probable that radiological investigations of cardiac and pulmonary pathology will soon change from purely static and anatomical methods to more physiological ones.

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AN APPROACH TO BRONCHOGRAPHY

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Bronchography is a valuable diagnostic procedure, but its use is restricted because of the time and specialised skill it requires. Moreover, the results obtained are frequently poor owing to incomplete filling of the lobar bronchi on the one hand and to filling of the alveoli on the other. With viscous neohydriol, unless the radiographs are taken almost immediately, alveolar filling is almost certain to obscure the picture. Consequently, little or no time can be allowed for screening the patient or for careful and deliberate filling of all necessary bronchi. It was, therefore, with some enthusiasm that the technique of Houghton and Ramsay (1951) was tried. This consists in increasing the viscosity of viscous neohydriol to prevent alveolar filling. Ten grammes of finely powdered sulphanilamide are thoroughly mixed with 20 c.c. of viscous neohydriol immediately before use. Our experience supports the claims made for this mixture, but it has the disadvantage of tending to separate out and to block the syringes and catheters used in the procedure. However, when introducing the mixture (albeit with some difficulty) by the usual method over the back of the tongue, it was noticed that satisfactory bronchograms could be obtained if the radiographs were taken as much as half an hour after the introduction of the opaque medium. As a result it seemed that it would be possible to introduce the medium in the operating theatre through the bronchoscope, transport the patient to the X-ray Department, and still obtain a satisfactory bronchogram. Our attempts to do this in the past, using viscous neohydriol, had been useless owing to excessive alveolar filling. In this way a technique of bronchography through the bronchoscope was developed.

At this time the water-soluble bronchographic medium " Dionosil " was introduced by Glaxo. Experience with this substance showed that it was much more irritant to the bronchial mucosa than the neohydriol-sulphanilamide mixture. Later the oily preparation of " Dionosil " was put on the market, which proved to be much less irritating. However, oily " Dionosil " has too great a tendency to enter the alveoli, and although all trace of the medium will disappear from the lungs in a few days the bronchograms obtained are not of the best owing to the faint shadow cast by the medium and filling of the alveoli. The faintness of the shadows is particularly noticeable in fat people or when the bronchi to be outlined are behind the heart shadow or in an opaque lung, segment or lobe (see Fig. 1).

At present, therefore, it is our practice to add oily " Dionosil " to the sulphanilamide-neohydriol mixture to make it easier to handle. The proportions of each are about equal. The mixture does not enter the alveoli, is therefore completely eliminated by coughing and casts an excellent radiographic shadow (see Fig. 4).

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Technique of Selective Bronchography

Bronchography through the bronchoscope is particularly valuable in outlining selected localised areas of the bronchial tree, as will be discussed later. The method is as follows: after premedication with morphia and atropine the throat, larynx and trachea are anæsthetised, using 60 m. (3·5 ml.) of amethocaine. The bronchoscope is then passed, any excessive secretion or pus is carefully removed by suction and a thorough inspection is made of the bronchial tree. When it has been decided which bronchus or group of bronchi are to be filled the area is sprayed directly with amethocaine by means of Clerf's intrabronchial spray, and the excess is removed by suction. This manœuvre effectively counteracts any tendency to coughing. The opaque medium is then introduced by means of a Record syringe attached to a Chevalier Jackson suction tube (see Fig. 3). For the lower lobe and the middle lobe a straight suction tube is used, but for the upper lobes and the apical segments of the lower lobes a suction tube with a curved gum elastic end is used. However, if the curved end cannot be made to enter the appropriate bronchus it is quite sufficient to deposit the opaque medium at the entrance of the bronchus, withdraw the bronchoscope, and then to put the patient in such a position as to allow the medium to flow into the bronchus. A volume of 2-10 c.c. of the opaque medium is used, depending on the area to be filled. The patient is then told to refrain from coughing, and is put on the trolley in the position required for retention of the opaque medium, and transported to the X-ray Department for antero-posterior and lateral radiographs. Following this he is returned to the ward or recovery room and the physiotherapist institutes postural drainage.

Bilateral Bronchography

Bilateral bronchography can also be successfully and conveniently combined with bronchoscopy by an extension of the method described above. About 15 c.c. of the opaque medium are injected into the left bronchial tree in the manner previously described, and then a narrow bore rubber tube, well lubricated both inside and outside, is introduced into the right main bronchus using a Chevalier Jackson bronchoscopic dilator with the gum elastic end screwed off as an introducer (see Fig. 3.) The bronchoscope is then withdrawn over the rubber tube, which is left in position in the right main bronchus. The patient is then suitably postured to distribute the medium evenly throughout the left bronchial tree, and is transported to the X-ray Department lying on the left side with the rubber tube *in situ*. Immediately after arrival fluoroscopy is carried out and postero-anterior and left lateral radiographs are taken. Next a further 15 c.c. of opaque medium are injected, this time down the rubber tube into the right bronchial tree. The medium is evenly distributed by further posturing, screening is repeated to ensure proper distribution, and oblique and postero-anterior films are taken. In this way very satisfactory bronchograms can be obtained, and the danger of swallowing the medium is eliminated.

It is preferable to fill the left side first because the rubber tube lies more comfortably in the right main bronchus than in the left, and occasionally if it

is inserted into the left main bronchus it may be coughed out and come to lie in the right side. If there is any doubt as to the position of the tube it can be withdrawn a little so that its lower end lies in the lower end of the trachea.

The presence of a soft narrow bore rubber tube passing through the larynx into the bronchial tree causes no discomfort, and if, through any unforeseen delay, the effect of the local anæsthetic is wearing off, a further 5 to 10 minims of amethocaine can be injected down the indwelling tube before inserting the medium into the right side.

Discussion

Many advantages of bronchography performed through the bronchoscope have become apparent after using this method in almost a hundred cases. In general, selective or localised bronchograms have been performed where possible—on the principle that the smaller the amount of opaque medium introduced the better, and this especially in elderly and bronchitic subjects. Two procedures are performed at the same sitting, and this, besides being an obvious advantage to the patient, saves a great deal of time for the medical staff and X-ray Department. Since the introduction of this method in this Unit, a vastly increased number of bronchograms have been performed.

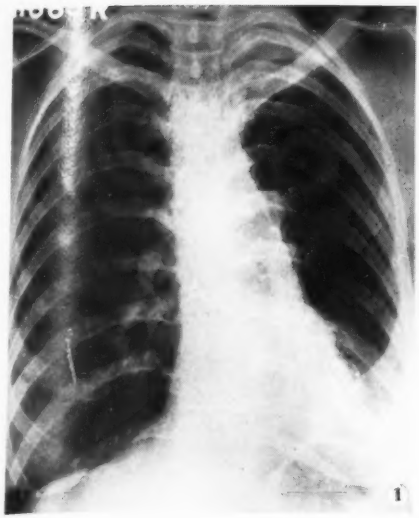
No pre-operative physiotherapy is necessary because secretions are removed by suction before introduction of the medium, and this type of bronchography can be performed in conjunction with routine out-patient bronchoscopies. Indeed the decision to introduce some opaque medium may be made only after the bronchoscope has been passed.

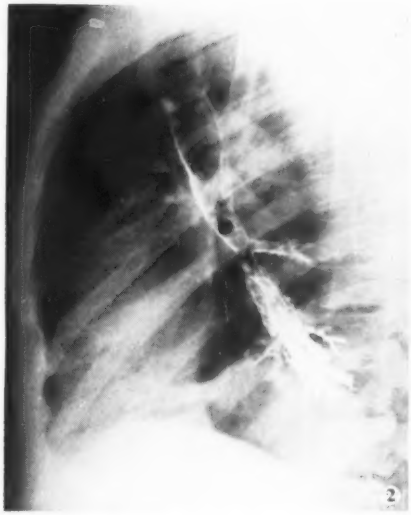
Accurate application of local anæsthetic to the precise bronchi to be filled, by means of Clerf's intrabronchial spray, ensures complete freedom from coughing in almost 100 per cent. of patients, except when the irritant watery Dionosil is used.

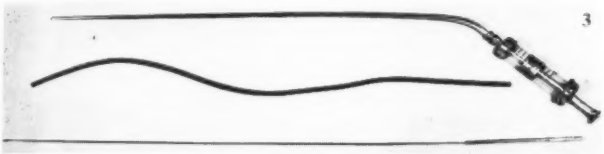
However, the success of bronchography through the bronchoscope is largely dependent on its performance under local anæsthesia, and therefore Units in the habit of employing general anæsthesia for bronchoscopy would probably find the method inconvenient, as it is necessary to transport the patient to the X-ray Department under anæsthesia accompanied by the anæsthetist and his machine. Moreover, the required posturing of unconscious adults is difficult. In children, therefore, where general anæsthesia must be used, we perform bronchography by the usual method through the intratracheal tube.

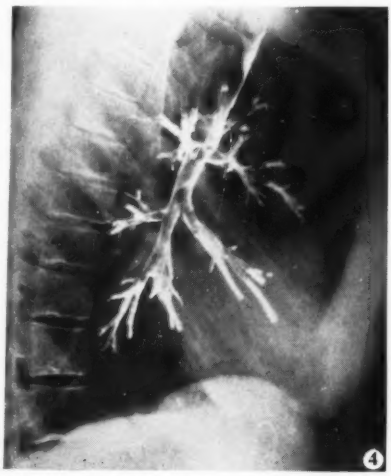
However, bearing in mind the foregoing limitations, it would appear that localised bronchography through the bronchoscope is a feasible proposition when the services of a skilled bronchoscopist are available.

At present bronchography for diagnostic purposes is employed extensively in this unit. It is used, as it were, to extend the range of vision of the bronchoscope. Suspicion of the presence of a neoplasm may be supported (see Fig. 5). In patients with unexplained hæmoptysis it has often been comforting to demonstrate small areas of bronchiectasis (see Fig. 2). In pulmonary tuberculosis oily Dionosil alone has been used so far, because if any Lipiodol is introduced into the mixture any alveolar filling which may occur on rare occasions would render subsequent radiographs difficult of interpretation.









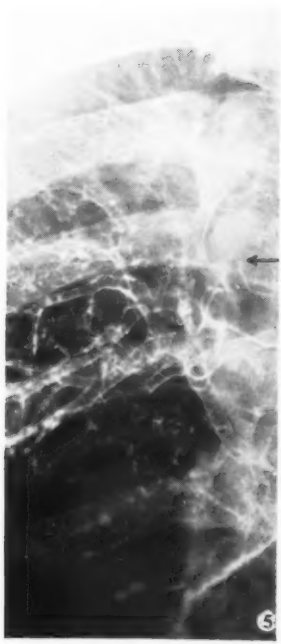


FIG. 1.—Selective localized bronchogram showing cylindrical bronchiectasis left lower lobe and demonstrating poor shadow cast by oily Dionosil.

FIG. 2.—Localized bronchogram of left lower lobe showing bronchiectasis in a case of unexplained hæmoptysis.

FIG. 3.—Showing Chevalier Jackson suction tube with attached syringe for introduction of the opaque medium through the bronchoscope, and rubber tube with introducer.

FIG. 4.—Bronchogram right lung showing excellent radiographic shadow and absence of alveolar filling when the special mixture is used.

FIG. 5.—Localized bronchogram of right upper lobe showing stenosis of apical branch which was subsequently confirmed as being due to bronchial carcinoma.

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However, oily Dionosil, if its viscosity and radiopacity could be increased by some means, would be an ideal opaque medium.

Summary

A technique of bronchography performed through the bronchoscope, designed to fill any or all the segments of one or both lungs at the same time, is described. Its advantages and disadvantages are discussed, together with the merits and demerits of various opaque media. It is suggested that by adding the diagnostic possibilities of bronchography to those of bronchoscopy this method can increase the number of cases in which a diagnosis can be made at an endoscopy clinic. Further, the easier performance of bronchography by this method allows of its application to a far greater number of cases than formerly.

My thanks are due to Mr. J. S. Davidson for his constant encouragement and invaluable advice, and to Mr. P. Harrison of the Department of Photography for the reproduction of the radiographs.

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STREPTOMYCIN IN TUBERCULOUS MENINGITIS AND MILIARY TUBERCULOSIS

A FIVE-YEAR SURVEY

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This paper, gives the results of streptomycin treatment over a period of five years of 78 cases, 63 with tuberculous meningitis and 15 with miliary tuberculosis alone.

It was clear that there would be insufficient material to compare different treatment schedules. A method involving continuous treatment was selected and has been retained practically without modification. All cases receive one daily injection of intramuscular streptomycin for six months and those with meningitis a sixteen-week course of intrathecal streptomycin, daily for the first week and thereafter every other day. It was thought that intensive short courses interspersed with, say, monthly intervals might have two disadvantages, firstly, the encouragement of drug-resistant organisms, and secondly, loss of morale each time patients resumed lumbar punctures.

Intramuscular dosages were 1 gramme daily over age 14, 0·5-0·75 gm. in the 5-14 age group and 0·5 gm. under 5. The corresponding intrathecal dosages were 0·1, 0·05-0·075 and 0·025-0·05 gm. All cases save one received intramuscular treatment, the injections being given into the vastus lateralis. Case 59 (male aged 6) was in a complete hip spica and, the condition being mild, was given oral isoniazide instead without ill effect. Four cases developed spinal block and required cisternal punctures under general anæsthesia (vinesthene or trilene). One of these was traumatic in origin from excessive struggling. Thereafter, apprehensive patients were given a general anæsthetic, there being five such cases.

Results of Treatment

The detailed results appear in Table I. The classification A, B and C denotes mild, intermediate and severe cases at the start of therapy. Mild cases (A) showed few symptoms but an abnormal cerebrospinal fluid (C.S.F.). Intermediate cases (B) while conscious had unmistakable meningitis with drowsiness and irritability, while severe cases (C) were stuporose.

Table II summarises each group and confirms general experience of the importance of early diagnosis, the mortality in groups A, B and C being 13·3, 44·4 and 81·5 per cent. respectively. The presence of an associated miliary infection does not seem to have influenced the prognosis. Table III, presenting the age incidences of the infection, reflects the unfavourable prognosis for infants.

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Diagnosis

Early diagnosis is both essential and difficult, taxing the powers of the ablest physician. Delay is fatal, but unnecessary treatment inflicts hardship, is sometimes disabling and always expensive. A short course of "blind" treatment, sometimes effected, followed by a pause during which a recrudescence or relapse is awaited to clinch a doubtful diagnosis, is thoroughly bad; though doubtless but a symptom of one of the most pernicious trends in modern medicine—that of using the powerful therapeutic reagents now available with little or no attempt at previous diagnosis. The risks of inducing streptomycin resistance or of facilitating the further organisation of dense exudate with increased liability of hydrocephalus are too great. Had case 20 received a full course of treatment in the first instance instead of a mere half-dozen injections, the fatal relapse and recrudescence might never have occurred.

An excellent account of the salient clinical findings was given by Rubie and Mohun (1949). There is usually a prodromal period averaging about three weeks. The duration of the prodromal phase seems of little prognostic significance. For this reason it does not figure in Table I. It is the condition of the patient at the start of treatment that is of paramount importance and every effort must be made to clinch the diagnosis before excessive deterioration sets in. Important prodromal symptoms are irritability, loss of interest generally, undue fatigue, poor appetite and failure to gain weight, digestive disturbances and fever. If to these be added headache and vomiting, full investigation is essential. Indeed, fever clinicians have for years recognised the advisability of lumbar puncture in any child who remains vaguely unwell for more than two to four days, as even a pyogenic meningitis may remain latent apart, perhaps, from a bulging fontanelle in infants. At this stage the C.S.F. may be almost normal, as in case 49, who for three weeks, apart from ten lymphocytes, had a normal C.S.F. and then developed a very acute meningitis. Tubercle bacilli were recovered from the C.S.F. despite a sugar content never lower than 50 mgm.

Convulsions often mark the onset and tetanic fits should be regarded with particular suspicion. These latter are a form of cerebellar fit and do not respond to calcium. (True rickets and tetany must be ruled out—there have been three such cases here in the last two years.) Infantile hemiplegia and spastic or flaccid paralyses sometimes occur.

Attention must be paid to recent contacts with open cases of tuberculosis (27 or 42·9 per cent. in this series) and also to a past history of tuberculous manifestations such as pleural effusion or erythema nodosum in the patient.

Meningitis being established, the differential diagnosis includes more immediately: lymphocytic meningitis, poliomyelitis, glandular fever, mumps meningitis, encephalomyelitis, virus pneumonia *encephalitis*, Weil's disease, *Canicola* fever and syphilitic meningitis. Rarer causes calling for no further comment include hepatic failure, uræmia, typhoid meningitis, trypanosomiasis, yeast meningitis, arsenical or lead encephalopathies, and occasionally cerebral hæmorrhage, abscess and tumour. In doubtful cases, tests germane to the diagnosis of Weil's disease, Canicola fever, glandular fever, syphilis and virus pneumonia should be done at once. The recent history or presence of a

parotid or submandibular swelling should betray mumps meningitis. A coincident or antecedent infection points to encephalomyelitis, especially in the occasional case with a considerably abnormal C.S.F. In lymphocytic meningitis there is no comparable prodromal period and the onset is abrupt. The course is relatively short, but the natural remissions of tuberculous meningitis may cause confusion. In the benign disease, the cell count in the C.S.F. tends to be higher, but is quite unreliable from a diagnostic viewpoint.

The combination of pains in the limbs and back, meningitis, and above all an unclouded intellect, strongly suggest poliomyelitis, but conversely a flaccid paralysis without clinical evidence of meningitis in Koch's meningitis may cause confusion, as in the following case.

Case 46, male aged 3, was admitted with a history of three days' vomiting and malaise, five days of comparative well-being, and lastly two days with inability to stand or move his right arm. Examination showed normal mentality, slight neck stiffness and flaccid paralysis of right arm and leg. C.S.F. showed: cells (L) 144, protein 50 mgm., chlorides 700 mgm., sugar 52 mgm. A diagnosis was made of " Undoubted A.P.M." There was no change for eight days, when, following tetanic spasms, his condition deteriorated and the flaccid paralysis became spastic. C.S.F. showed: cells 125 (L), protein 100 mgm., chlorides 620 mgm. and sugar 26 mgm. Despite streptomycin, he was dead within a further week.

The presence of tubercle bacilli in the C.S.F. is diagnostic, but these were found only in 10 cases (16 per cent.) from direct smear. Although in a further 42 cases the organisms were recovered from culture or guinea-pig inoculation (making a total of 52 cases or 82·5 per cent.), this is far too late for diagnostic purposes. There is no other absolute diagnostic criterion, but reduction (not absence) of sugar is the next most valuable finding. Rubie and Mohun (1949) give a suggested minimum figure of 45 mgm. per cent. for normal sugar content. This is undoubtedly of great significance, but in 4 of these cases the minimum finding was over 50 mgm. Consequently, a normal C.S.F. sugar does not invariably exclude tuberculous meningitis, but a figure as low as 30 mgm. strongly favours it. McLean (1936) pointed out that convulsions will temporarily elevate both the blood and later the C.S.F. sugar levels. The fall in chlorides is usually too late to be of diagnostic help and is consequently associated with extremely ill cases. In 16 of the 29 fatalities in this hospital the final reading was under 620 mgm.

Apart from lumbar puncture, X-ray examination of the chest to exclude miliary tuberculosis, pulmonary tuberculosis or a primary complex and Mantoux testing (1 in 10,000) are essential. Being strengthened in the previously held view that the importance of the Mantoux reaction was exaggerated by finding it negative in 6 of the first 10 cases in this series, I am now inclined to think insufficient use has been made of it here. Speed in investigation and diagnosis is essential, though too frequent lumbar punctures (more than once daily) are to be deprecated.

Case 39, female aged 36, from a farm, proved very difficult and the delay in diagnosis was probably fatal. Three months earlier she had erythema nodosum and X-ray showed an old calcified right apical focus. Ten days

before admission she had variable frontal headaches and vomiting, and after three or four days of relief, a renewal of symptoms with severe back and limb pains on the day before admission. Examination showed no signs of meningitis, normal and alert mental state, weakness of left quadriceps with absent knee-jerk and positive Amoss sign. A provisional diagnosis of poliomyelitis was made. The white blood count was 18,000 (P. 83 per cent., L. 14 per cent., M. 3 per cent.), urine contained albumin and red cells and C.S.F. showed: cells 402 (L), protein 100 mgm., globulin nil, chlorides 700 mgm. and sugar 75 mgm., W.R. negative, also in blood. Chest X-ray showed old lesion only and Mantoux was positive 1 in 10,000. Three days later she felt better and the C.S.F. was unchanged, but by the seventh day had developed a very severe headache. The leucocyte count was now 15,000, Paul Bunnell negative, blood urea 30 mgm., while C.S.F. showed: cells 210 (L), protein 450 mgm., chlorides 700 mgm. and sugar 50 mgm. On the eighth day, C.S.F.: cells 96 (L), protein 200 mgm., chlorides 700 and sugar 75 mgm. Clinical condition was again improved and the laboratory requested a further specimen of blood, the agglutination test for Weil's disease having proved equivocal. On the ninth day she was less well and mentally confused, C.S.F. showing: cells 385 (L), protein 320 mgm., chlorides 600 mgm. and sugar 86 mgm. Full treatment with streptomycin was started, but she died on the fifteenth day, autopsy revealing early tuberculous meningitis with a mild degree of hydrocephalus. C.S.F. sugar on the day before death was 75 mgm. Clearly, more attention should have been paid to the history and to the improbability of Weil's disease causing paralyses.

Discussion of Treatment Results

For purposes of comparison, the classification set out by Robertson and Gairdner (1952) has been adopted.

(1) *Rapid Recovery.* Ten cases (9 in category A, thus stressing the advantage of early diagnosis, and 1 in category B) made remarkable recoveries, appearing clinically normal within a month and having C.S.F. approximating to normal. "One gets the impression . . . that long treatment may not be necessary" (Robinson and Gairdner, 1952). This needs courage and has not yet been tried here.

(2) *Rapid Fatalities and Decerebrate Rigidity.* Fifteen cases, 13 in category C and 2 in category B on admission, rapidly deteriorated and died. Five cases developed decerebrate rigidity and 1 recovered, thereby showing that miracles happen even in medicine.

Case 41, male, aged eleven months, was admitted, tubercle bacilli having already been found in the C.S.F. elsewhere. He had miliary tuberculosis also and had slept in the same bed as his mother, who had open pulmonary tuberculosis. He was semi-comatose and spastic with marked head retraction. Standard treatment was begun (25 mgm. streptomycin intrathecally), but he became so ill that all treatment was stopped on the forty-fifth day, the prognosis being considered hopeless. Marked rigidity, extreme opisthotonos with head all but touching the buttocks, grinding teeth, extensor tonic spasms, a frequent piercing cry and generalised wasting denoted decerebrate rigidity. C.S.F. showed: cells 69, protein 120 mgm., chlorides 600 mgm., sugar 25 mgm. For three weeks he remained like this, but after a further three weeks had improved somewhat, the C.S.F. findings now being: cells 7 (L), protein 60 mgm., chlorides 720 mgm. and sugar 46 mgm. Treatment was cautiously resumed,

TABLE I.—MENINGITIS

Case No.	Severity	Age	Sex	Chest X-ray	Days in Hospital: Before diagnosis	Days in Hospital: Total stay	Drugs	Outcome	Subsequent follow-up	Last C.S.F. before death or discharge: Cells	Protein	Chlorides	Sugar	Lowest C.S.F. sugar	T.B. in C.S.F.	Known contacts	Notes
1	B	9	F.	C.	2	212	S.	F.	Nil	43	70	620	Absent	Nil	+	+	Satisfactory response; later recrudescence.
2	B	11	F.	C.	3	380	S.	S.	3½Y.	9	40	730	50	Nil	+	+	Initial pleurisy; good response.
3	B	2	F.	P.C.	5	22	S.	F.	Nil	110	80	660	Nil	Nil	+	—	Pertussis and L. abducent palsy.
4	A	19	F.	M.	2	289	S.	S.	3½Y.	Nil	6	720	48	37	+	+	Now married and well.
5	C	6	M.	Nil	11	38	S.	F.	Nil	270	140	620	10	10	+	—	
6	A	28	F.	C.	2	332	S.	S.	3Y.	4	20	720	39	Nil	+	+	Tuberculous pyosalpinx one year before.
7	B	7/12	F.	C.	4	47	S.	F.	Nil	30	2000	780	18	Nil	+	+	"Tetany"—decerebrate rigidity.
8	B	18/12	M.	C.	3	320	S.	S.	2½Y.	4	40	690	57	31	+	—	
9	B	5	M.	C.	4	290	S.	S.	3Y.	5	30	700	54	24	+	+	Cisternal punctures owing to spinal block. Developed Pott's disease.
10	B	16	F.	C.	2	259	S.	S.	2¾Y.	6	80	740	46	29	+	+	Pleural effusion two years previously.
11	B	10	F.	C.	2	635	S.	F-R(2)	1½	7	70	740	50	Nil	+	—	Died hydrocephalus fourth ventricle.
12	B	39	F.	C.	1	9	S.	F.	Nil	232	200	660	30	30	+	—	L. pneumonectomy one year before. Insensitive to streptomycin.
13	B	42	F.	C.	1	367	S.	S.	2Y.	3	70	740	44	20	+	—	Deaf. Tuberculous sacro-iliac joint.
14	B	10/12	F.	—	7	38	S.	F.	Nil	260	200	620	27	27	+	+	Started flaccid paralysis L. leg. Decerebrate rigidity.
15	A	16	M.	M.	13	540	S.P.	S.R.	1¼Y.	4	40	740	56	31	+	—	Miliary—thirteen days' delay in diagnosing meningitis, relapse two months after end of first course.
16	B	2	F.	C.	4	115	S.P.	F.	Nil	84	250	620	34	30	+	—	
17	B	57	M.	M.	10	180	S.P.	S.	2½Y.	4	45	720	53	14	+	—	Had previous silicosis; began with tuberculous laryngitis.
18	C	43	M.	P.T.	2	15	S.P.	F.	Nil	186	360	580	27	27	+	—	Had R. hemiplegia.
19	A	21	M.	P.T.	1	266	S.P.	S.	2¼Y.	7	90	670	63	26	—	—	Positive sputum; pneumoperitoneum.

20	B	3	F.	C.	1	244	S.P.	S.	$\frac{3}{52}$	10	70	720	50	20	—	+	Had about five injections nine months previously in another hospital as therapeutic test, diagnosis being uncertain.
,,		4	F.	C.	4	25	S.P.	F.	Nil	105	250	660	31	31	—	+	Relapsed again and died.
21	C	5	M.	P.C.	14	30	S.P.	F.	Nil	162	400	560	37	Nil	+	+	For ten days was thought to have poliomyelitis.
22	C	$\frac{5}{12}$	F.	P.C.	3	57	S.	F.	Nil	225	500	660	20	20	+	+	Decerebrate rigidity.
23	A	51	M.	M.	3	374	S.P.	F.	$\frac{5}{12}$	9	100	720	53	31	+	—	Died from hæmoptysis; had renal T.B.
24	B	6	M.	C.	2	187	S.	S.	2Y.	7	60	710	44	44	—	+	Pott's disease spine, two years before. Spinal block—cisternal punctures—C.S.F. normal three months after discharge.
25	C	$\frac{11}{12}$	M.	—	10	34	S.	F.	Nil	56	60	660	31	31	+	+	Left infantile hemiplegia.
26	C	16	F.	C.	1	45	S.P.	F.	Nil	950	250	600	40	38	+	—	Bilateral sixth nerve and L. third nerve palsies on admission.
27	C	2	F.	M.	1	504	S.P.	S.	$1\frac{1}{4}$Y.	3	20	720	54	24	+	+	Had pleural effusion and after treatment, tuberculous cervical adenitis. Became deaf and now at special school.
28	A	19	F.	C.	1	241	S.P.	S.	$1\frac{1}{2}$Y.	6	50	720	82	28	—	—	Fully treated miliary T.B. one year previously (elsewhere).
29	A	2	M.	C.	2	232	S.P.	S.	1Y.	12	40	710	49	43	+	+	
30	A	$1\frac{1}{2}$	M.	C.	2	199	S.P.	S.	1Y.	13	40	740	41	39	+	+	
31	A	3	M.	C.	1	182	S.P.	S.	2Y.	1	40	720	57	42	—	—	
32	B	6	M.	C.	3	272	S.P.	S.	$1\frac{1}{2}$Y.	5	30	710	53	30	—	—	L. oculomotor paralysis. R. arm spastic paralysis.
33	B	28	F.	M.	2	120	S.P.	F.	2Y.	15	200	660	60	52	+	—	Developed schizophrenia—familial complaint and died recently of pulmonary tuberculosis. C.S.F. reported normal.
34	C	43	M.	P.T.	1	14	S.P.	F.	Nil	15	160	740	63	63	+	—	Old case of pulmonary tuberculosis—treated successfully two years before at same hospital. Had right hemiplegia.
35	B	6	F.	C.	4	519	S.P.	S.	1Y.	3	20	710	62	30	+	—	Initial C.S.F. 56.
36	B	8	M.	C.	1	323	S.P.	S.	$1\frac{1}{4}$Y.	18	70	720	46	46	+	—	Ptosis L. eye on admission.
37	B	6	F.	C.	1	273	S.P.	S.	$1\frac{1}{2}$Y.	1	20	720	53	32	+	—	

TABLE I.—MENINGITIS (*continued*)

Case No.	Severity	Age	Sex	Chest X-ray	Days in Hospital: Before diagnosis	Days in Hospital: Total stay	Days in Hospital: Drugs	Days in Hospital: Outcome	Days in Hospital: Subsequent follow-up	Last C.S.F. before death or discharge: Cells	Protein	Chlorides	Sugar	Lowest C.S.F. sugar	T.B. in C.S.F.	Known contacts	Notes
38	B	15	F.	M.	3	673	S.P.	S.	1Y.	4	30	720	53	32	+	—	L. sixth nerve palsy. Last C.S.F. before first recrudescence.
										100	60	720	28	28	+	—	At onset of first recrudescence.
										17	60	720	50				Before second recrudescence.
										105	150	720	36	36	+	—	At onset of second recrudescence.
									$\frac{5}{12}$	3	35	720	50				On discharge—well $\frac{5}{12}$ later but deaf.
39	A	36	F.	C.	10	15	S.P.	F.	Nil	385	320	600	86	50	—	—	See text.
40	A	6	F.	C.	17	275	S.P.	S.	1½Y.	1	30	720	53	32	—	—	Relapse after treatment two years previously, from which deaf.
41	C	1	F.	M.	1	434	S.P.	S.	1Y.	5	30	760	25	25	+	+	Decerebrate rigidity. Recovered.
42	B	18	M.	C.	9	9	—	F.	—								Case quite atypical. Diagnosed only at autopsy.
43	C	16	F.	M.	1	3	S.	F.	—	512	100	585	29	29	+	—	Moribund on admission.
44	C	3	F.	—	1	1	—	F.	—	37	40	710	40	40	+	—	Died few hours after admission.
45	B	1½	F.	C.	1	379	S.P.	F.R.	—	46	100	720	32	20	+	—	Recrudescence four weeks after treatment
										190	1200	620	40	23	+	—	stopped; no response to second course.
46	B	3	M.	—	3	15	S.P.	F.	—	125	100	620	26	26	—	—	See Text.
47	A	46	M.	C.	6	214	S.P.	S.	1½Y.	6	50	730	68	43	+	—	Very rapid improvement.
48	A	22	F.	M.	6	259	S.P.	S.	1Y.	3	30	700	55	40	+	—	Moribund for several weeks.
49	A	5	F.	M.	22	280	S.P.	S.	$\frac{9}{12}$	5	30	720	63	50	+	—	On admission had almost normal C.S.F. with 10 lymphocytes for three weeks. Suddenly developed an acute meningitis. Rapid recovery.

50	C	6	M.	C.	1	22	S.P.	F.	—	126	100	480	30	30	+	+	T.B. right ankle four years before. Miliary T.B. (treated) three years before. Apparent tetany on admission.
51	C	33	M.	M. P.T.	1	17	S.P.	F.	—	68	250	700	30	30	+	+	Cavitation both lungs. Tuberculous epididymitis.
52	C	8	F.	C.	—	7	—	F.	—	57	8000	600	55	55	+	+	Erroneously thought to have Pott's disease and spinal compression. Tubercle bacilli isolated from guinea-pig only.
53	B	38	M.	M.	1	259	S.P.	S.	$\frac{1}{52}$	16	120	710	50	39	+	—	Tuberculous sacro-iliac joint. Deaf.
,,		39	M.	C.	1	194	S.P.	S.	$\frac{2}{12}$	284	250	680	41	41	+	—	Had cisternal punctures due to low spinal block.
										1	60	750	49				
54	C	6	M.	C.	2	201	S.P.	S.	$\frac{0}{12}$	30	100	700	53	42	+	+	Transferred for orthopædic treatment. T.B. knee and hip. Mentally retarded and has epilepsy.
55	C	2	M.	C.	2	36	S.P.	F.	—	180	100	700	34	18	+	+	Decerebrate rigidity.
56	B	8	M.	M.	2	270	S.P.	S.	$\frac{1}{12}$	3	40	720	74	44	+	+	
57	C	11	F.	C.	2	287	S.P.R.	S.	$\frac{2}{12}$	5	40	740	57	18	+	+	See Text.
58	B	7	M.	C.	3	119	S.P.	S.	$\frac{0}{12}$	115	350	680	35	35	—	+	T.B. L. hip. Transferred for treatment.
59	A	6	M.	C.	1	243	S.P.	S.	$\frac{2}{12}$	4	20	740	63	51	—	+	Previous T.B. R. hip.
60	C	1	F.	—	1	3	S.P.	F.	—	190	300	620	16	16	+	+	
61	C	$1\frac{1}{2}$	F.	—	2	7	S.P.R.	F.	—	80	800	575	10	10	—	—	
62	C	19	M.	C.	19	76	S.P.R.	F.	—	260	380	600	35	18	+	—	Admitted on twentieth day.
63	C	2	F.	—	2	5	S.P.R.	F.	—	200	200	620	18	18	+	—	

KEY: A. Early cases; B. Intermediate cases; C. Late cases.

Chest X-rays. C. Clear; M. Miliary; P.C. Primary complex; P.T. Pulmonary tuberculosis.

Drugs. S. Streptomycin; P. Para-aminosalicylic acid; R. Rimifon (isoniazide)

Outcome. S. Survival; F. Fatality; R. Recrudescence or relapse.

TABLE II.—ANALYSIS OF FATALITIES AND STAGE OF DISEASE

Admission state	*(Miliary)*	*Total*	*Mortality*	*(Miliary deaths)*	*Per cent. Mortality*
Early (A)	(4)	15	2	(1)	13·3
Intermediate (B)	(5)	27	12	(1)	44·4
Severe (C)	(4)	21	17	(3)	81·5
Totals	(13)	63	31	5 (36·5%)	49·2

TABLE III.—MORTALITY AND AGE INCIDENCE

Age group	*A*	*B*	*C*	*Total*	*A*	*B*	*C*	*Total*	*Per cent. Mortality*
0-3	2	6	8	16	0	5	6	11	68·8
3-14	5	11	6	22	0	4	5	9	40·9
Over 14	8	10	7	25	2	3	6	11	44
All groups ..	15	27	21	63	2	12	17	31	49·2
	Total admissions				Deaths				

TABLE IV.—DETAILS OF MILIARY CASES

Case No.	*Age and sex*	*Time in hospital*		*Drugs*	*Time for X-ray to clear*	*Out-come*	*Period of subsequent observation*	*Notes*
		Before Diagnosis	*Total*					
I	27 F.	1	343	S.	18W.	S.	4 years	
II	4 F.	5	275	S.	15W.	F.	—	Died cerebral tuberculoma
III	20 F.	1	295	S.	20W.	S.	3 years	
IV	31 M.	1	275	S.P.	12W.	S.	2¾ „	
V	16 F.	1	291	S.P.	17W.	S.	2½ „	
VI	16 F.	1	357	S.P.	24W.	S.	2½ „	
VII	16 F.	1	218	S.P.	16W.	S.	2 „	
VIII	23 M.	1	384	S.P.	34W.	S.	1½ „	
IX	6 F.	15	248	S.P.	16W.	S.	1¼ „	Deaf. See Text on diagnosis.
X	19 F.	2	248	S.P.	16W.	S.	1¼ „	
XI	25 F.	2	233	S.P.	14W.	S.	1¼ „	
XII	52 M.	1	30	S.P.	—	F.	—	No response; meningitis excluded.
XIII	6 F.	32	322	S.P.	26W.	S.	1 „	Notified and confirmed glandular fever. Miliary tuberculosis only found afterwards.
XIV	2 F.	1	294	S.P.	18W.	S.	6M.	
XV	13 M.	1	?	S.P.	18W.	?	—	Developed meningitis six weeks after cessation of treatment. Is again on full treatment and making good progress.

intramuscular at first and after two further months intrathecal on alternate days for three more months in all. Two weeks after second cessation of treatment C.S.F. was normal. Six months later he was discharged, slightly backward for his age, but now, after another year, has made up all leeway.

(3) *Cases with Unpredictable Progress.* These form the majority, many patients remaining extremely ill for weeks or months and then dying or recovering. All the surviving cases in this series had given clear indication of improvement by the end of four months. If the outcome had still remained uncertain, prolongation of treatment might well have been desirable even for a whole year. "It is in this group that one feels the need of adjuvants to streptomycin" (Robertson and Gairdner, 1952). The immediate possibility is isoniazide.

Case 57, female, aged 11, a tuberculosis contact, was admitted with advanced clinical tuberculous meningitis. C.S.F. showed: cells 420 (mainly L), protein 410, chlorides 585, sugar 18 mgm. per cent., tubercle bacilli present. Standard treatment was given. Her condition got steadily worse. On the nineteenth day, oral isoniazide (rimifon) was begun, 50 mgm. Q.D.S. On the twenty-fourth day severe carpo-pedal spasms occurred. Intrathecal isoniazide was given, 50 mgm. every other day, alternating with streptomycin. A month later, with an unconscious, spastic, incontinent patient who was wasted, had severe contractures from hamstring spasm and emitted a meningitic cry through grinding teeth, the prognosis appeared hopeless. Various ancillary methods of treatment such as surgery and P.P.D. were contemplated, but as after another month there was a marked improvement, nothing further was done. Treatment was discontinued as usual, following which recovery was uninterrupted until her discharge from hospital six months later. Even when her general condition was at its worst there was an improvement in the C.S.F.: cells 25 (L), protein 160 mgm., chlorides 700 mgm. and sugar 50 mgm. Presumably, such a trend can be regarded as a favourable sign in an otherwise apparently hopeless case.

It is a plausible assumption that isoniazide saved this child, but since the deterioration continued for six weeks after it was first used and streptomycin cases behave similarly, there can be no definite conclusion. Had surgery or P.P.D. been used, it would have been tempting to ascribe to them her recovery, though, again, either might in so ill a patient have been lethal. Except when an obvious block is present, the indications for surgery seem very difficult to define because of the difficulty in forecasting the course of any particular case. In fact, partly because the nearest neurosurgical centre is 120 miles away, none of these cases have had any surgery, and although this series is too small for statistical comparisons, the results, taken at face value, do not seem inferior to those generally reported.

Relapses and Final Results

Four cases had one relapse each, with two fatalities. Two others had two recrudescences. One of them, case 38, is now well. The other, case 11, died suddenly during a tetanic (cerebellar) fit one month after being discharged from hospital. Autopsy showed fourth ventricle hydrocephalus due to non-specific arachnoiditis (*i.e.*, fibrosis of scar tissue) causing a block. The tuberculous process had been arrested. In addition, two further patients among the

fourteen at present under treatment but not included in this series have relapsed.

Of the survivors, eight were discharged with abnormal C.S.F.s, two to other hospitals and six to their homes. Three of these latter had normal fluids three months later, but the others lived too far away for readmission. They have remained well. Only in special cases are patients readmitted for lumbar punctures. Instead, their doctors or chest physicians are asked to refer them back only in the event of symptoms suggestive of relapse, notably pyrexia, unsatisfactory weight, headache or vomiting.

Twenty-nine deaths occurred in the hospital and two after discharge, case 33 two years later from pulmonary tuberculosis and case 23 four months after from hæmoptysis.

One child developed Pott's disease of the spine three weeks after discharge. Two adults had unilateral sacro-iliac tuberculosis, two children developed hip and one a knee infection. This last mentioned also shows gross mental deterioration, fortunately the only one in the series. All the others were well up to two or three months ago.

The notes of a case, mislaid in another hospital, have just been returned too late for inclusion in the tables. A boy aged 15, category B, was successfully treated for meningitis, but after a year developed Pott's disease of the lower thoracic spine. It is learned that, one year after, he has just gone home and will require out-patient treatment only. He remains apparently well.

Miliary Tuberculosis

There were 15 cases of miliary tuberculosis, 2 of whom died and 1 (case XV) has developed tuberculous meningitis six weeks after the cessation of treatment. The first death (case II) was from cerebral tuberculoma and the second (case XII) a primary treatment failure without meningitis. The mortality rate is thus 13·3 per cent. and the failure rate of treatment 20 per cent.

Every case of miliary tuberculosis should have a lumbar puncture directly the diagnosis is made, and this should be repeated from time to time during treatment or whenever progress seems unsatisfactory. This was not realised at first until, in one case of apparent miliary tuberculosis (case 13), an associated meningitis was discovered after thirteen days.

Radiological changes can appear very quickly. Case IX was admitted as P.U.O. and fully investigated as such, beginning with an X-ray of the chest which was normal. Two weeks later, a repeat film showed the presence of a typical snowstorm.

Toxic Effects of Streptomycin

Apart from 7 cases of deafness, one in a patient still under treatment and therefore excluded from this series, there were no troublesome reactions. Six of these cases resulted from dihydrostreptomycin, which was immediately discontinued.

Summary

(1) The results of the streptomycin treatment of 63 cases of tuberculous meningitis and 15 of miliary tuberculosis over five years are presented.

(2) The need for early diagnosis of tuberculous meningitis is discussed. The significance of C.S.F. changes, especially sugar, is considered.

(3) The response to treatment is classified and discussed.

Every case of miliary tuberculosis should have a lumbar puncture on diagnosis and at intervals thereafter, to exclude possible association with latent meningitis.

The most grateful thanks are due to Dr. B. L. Moore of the Public Health Laboratory, Dixie's Field, Exeter, who carried out all the laboratory work in connection with the above cases. Without his skilled and willing co-operation the work would have been at a great disadvantage. My thanks are due to my colleague Dr. D. F. Johnstone for looking after some of the cases and also to Drs. D. Levet, D. Parken, K. MacGregor, J. Hales, M. D. Youings and D. Powell, who have all at different times been associated with me.

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ADDENDUM

All our patients now receive oral (but not intrathecal) isoniazide as well as streptomycin and P.A.S., but the period of surveillance is too short for comparison.

SOME OBSERVATIONS ON A CASE OF DIFFUSE INTERSTITIAL FIBROSIS OF THE LUNGS

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In 1944 Hamman and Rich described four cases of a fatal pulmonary disease, characterised by increasing breathlessness, which they called acute diffuse interstitial fibrosis of the lungs. Histologically the changes in the lungs varied from acute congestion and œdema with hyaline membrane formations to extensive fibrosis of the alveolar walls. Similar cases have since been reported by Eder, Hawn and Thorn (1945), Potter and Gerber (1948), Beams and Harmos (1949), Golden and Tullis (1949), Katz and Auerbach (1949) in the United States; Ferrar, Carebarrere, Bottinelli, Mendilaharsa and Giudice (1949) in Uruguay; and Heppleston (1951) in Great Britain. The lesions on the whole appear to have been fairly consistent, but some of the subsequent cases have been less acute than those described by Hamman and Rich. The case which we now wish to present ran a chronic course, but terminated acutely and produced a wide range of pulmonary changes in which it was possible to trace its pathogenesis.

Clinical History and Findings

A young married man aged 35 worked a small mixed farm and was in good health until the beginning of 1951, when he began to notice increasing breathlessness. This was and remained his sole symptom, and as he had no cough, did not lose weight or suffer from any general weakness, he wondered if he were imagining his disability, and struggled on with his work. Eventually he sought medical advice and an X-ray was taken (April 1951), and reported as suspected pneumoconiosis, the slight changes consisting of small, ill-defined opacities widely scattered throughout the lung fields. A second film, however, taken one month later, was reported as normal and the original tentative diagnosis was withdrawn. In view of this second X-ray and the absence of physical signs he was regarded as being neurotic and it was decided that a short holiday was advisable.

He had returned from this holiday about forty-eight hours before he was first seen at his home by one of us (A.G.O.) who is responsible for this account of his illness. During the twelve-mile journey home he had driven the car himself, although he was complaining of a tight feeling in his chest, and on his return he appeared to be worse rather than better from the change. That night he was breathless at rest for the first time and the next morning this prevented him from getting up and made him prefer to lie flat rather than to sit upright. He developed a cough with frothy phlegm and noticed a " bubbling

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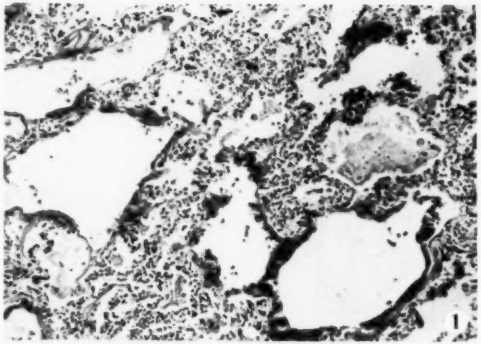

FIG. 1.—Alveoli showing darkly stained hyaline membranes on their walls. A little flocculent material derived from œdema fluid is also present in some other alveoli.
H & E, ×90.

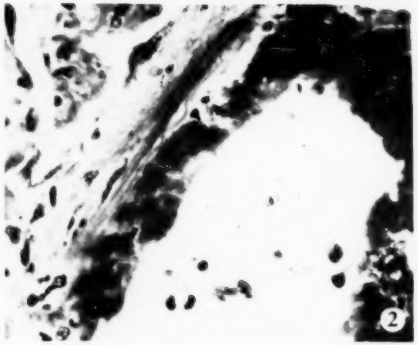

FIG. 2.—Hyaline membrane showing early organization with unchanged hyaline substance on the free surface merging into new fibrous tissue on the alveolar wall.
H & E, ×575.

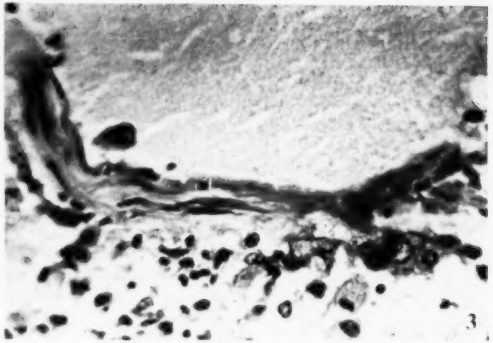

FIG. 3.—More advanced organization of hyaline membrane with infiltration by connective tissue cells along its length.
H & E, ×410.

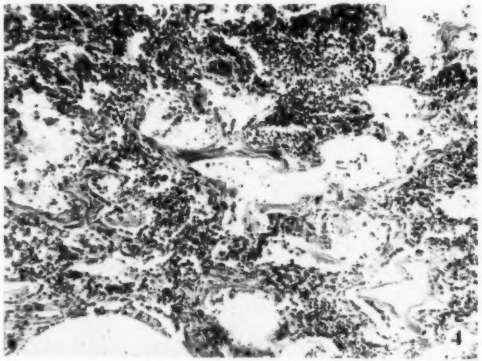

FIG. 4.—An area where the hyaline membranes have been completely replaced by fibrous tissue.
H & E, ×90.

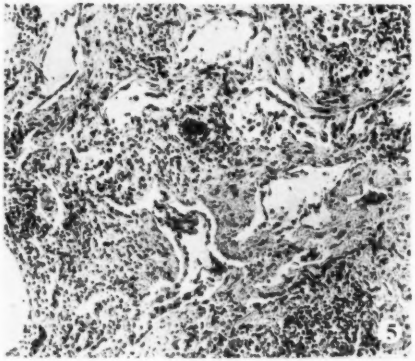

FIG. 5.—More advanced fibrosis with new formed alveolar linings.
H & E, ×100.

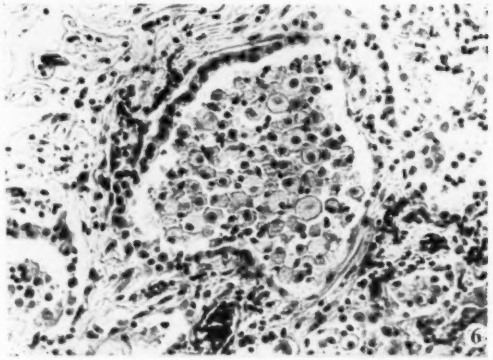

FIG. 6.—An alveolus with a cuboidal cell lining containing lipophages.
H & E, ×225.

PLATE XXI

feeling" in his chest, and he so deteriorated over the next night that when he was seen the following afternoon (June 9, 1951) he presented a distressing picture. He was lying in bed, intensely cyanosed and semi-conscious, with the most extreme degree of dyspnœa that the writer has seen. The respiration rate at rest on his back was 40 per minute, and when an attempt was made to raise him into a sitting position to examine the back of his chest a most alarming increase in the respiratory rate and the respiratory distress caused the procedure to be abandoned immediately. The neck veins were grossly dilated and the pulse rate was 140 per minute, but the most striking physical sign was a squelching sound which occurred with respiration and could be heard clearly some distance from the bed. When the chest was examined this squelching was heard equally with inspiration and expiration and was so loud that it obliterated the heart sounds. The only other signs were slight œdema of the sacrum and ankles and a palpable liver. The opinion was expressed that the condition was hopeless, but, as the parents were loth to accept this, admission to hospital was arranged. In hospital his condition steadily deteriorated and he died at noon on the following day; within seventy-two hours of his twelve-mile drive home from holiday.

Morbid Anatomy and Histology

The only significant abnormalities were in the lungs, the right weighing 640 grammes and the left 600 grammes. The trachea was congested and contained frothy mucus and there were a few patches of fibrinous exudate on the pleuræ. Both lungs were firm and on section showed a reticulated greyish-red appearance resembling consolidation throughout. Microscopically the changes varied from one area to another, depending on the stage of the disease, but the outstanding one was a diffuse fibrosis of the alveolar walls. There were, however, more acute changes superimposed consisting of hyperæmia and œdema with, in many parts, hyaline membrane formations closely applied to the alveolar walls (Fig. 1). These membranes were eosinophilic in staining reaction, but frozen sections showed variable amounts of fat.

Amongst the membranes there were many examples showing no clear-cut line of demarcation between the hyaline substance and the underlying connective tissue of the vesicle walls. Instead there was a gradual transition from hyaline substance to recently formed fibrous tissue (Fig. 2), whilst some of the membranes appeared actually to be infiltrated by fibroblasts (Fig. 3). This, together with the fact that the distribution of the hyaline membranes corresponded so closely with that of newly formed fibrous tissue (Fig. 4), convinced us that the hyaline substance was being transformed into collagen by a process of organisation, thus producing a generalised fibrosis of the lungs. In many areas where the fibrosis was most marked there was an alveolar lining of flattened or cuboidal cells (Fig. 5), and in these parts the alveoli were sometimes filled with fat-laden phagocytes (Fig. 6). There were also foci of inflammatory cell infiltration of the alveolar walls in some places with lymphocytes predominating (Fig. 2), and there was an increase of lymphoid tissue in some of the subpleural lymph follicles. Small infiltrations of lymphocytes, endothelial cells and multinucleated giant cells of foreign-body type were also

cell lining containing lipophages. H & E, ×225.

new formed alveolar linings. H & E, ×100.

membranes have been completely replaced by fibrous tissue. H & E, ×90.

seen, but there were no tubercle bacilli or other bacteria to be found, nor were inclusion bodies demonstrable. In a few of the less fibrotic areas there was some emphysema.

Discussion

This strange history with its dramatic termination was the cause of much speculation until the full pathological picture was unveiled. It is, in fact, only in this way that the disease can be recognised at the present time, although it may be suspected clinically. The invariable and basic symptom is an increasing breathlessness, but the variation in the reported clinical findings has made it difficult to establish a recognisable syndrome. The breathlessness is usually accompanied by other symptoms such as paroxysmal cough, cyanosis, increasing weakness and emaciation, but our patient is the only one so far reported in whom slowly progressive dyspnœa was the sole symptom and in whom physical signs were completely absent until the last forty-eight hours of life. The rate at which the disease proceeds fluctuates, but death is always the ultimate outcome, either by cor pulmonale or by simple suffocation. No characteristic radiological changes have been recognised, and this is not surprising considering the variations in the degree and distribution of the œdema during the progress of the disease.

Hyaline membranes similar to those seen in this condition have been noted in other inflammatory conditions (Farber and Wilson, 1932) usually associated with an exudate, and Heppleston (1951) has suggested that they are formed by a condensation of the exudate under the pressure of inspired air. Although Hamman and Rich (1944) noticed organisation of hyaline membranes they did not stress its importance and they believed that the new formed fibrous tissue originated within the alveolar walls rather than on the surface. Other observers have accepted their interpretation, except Heppleston (1951), who considered that organisation of the hyaline membranes might be responsible for the fibrosis. From the evidence we have obtained we consider that this is, in fact, the essential process.

The disease is likely to be either a virus infection or an allergic phenomenon (Hamman and Rich, 1944). Whilst studying typical inflammatory reactions in the lungs, Geever, Neuberger and Rutledge noticed localised lesions with histological appearances resembling diffuse interstitial fibrosis, and they suggested that the disease might not be as uncommon as is usually thought. It is possible that localised forms occur and result in the small areas of interstitial fibrosis occasionally seen in otherwise normal lungs, but in disregarding the essentially diffuse nature of the lesion there is a danger that it will become confused with other unusual pulmonary reactions.

Summary

A case of diffuse interstitial fibrosis of the lungs running a chronic course and terminating in an acute exacerbation is reported.

The especial interest and value of this case, in our view, lies in the fact that while it began insidiously and followed a chronic course for some months, the

acute terminal phase was rapidly fatal, causing death in less than seventy-two hours. A particularly favourable opportunity was thus presented of examining and comparing the acute and chronic phases of the disease, and this has led to the presentation of a theory of pathogenesis. It is suggested that the interstitial fibrosis is derived from the organisation of the hyaline membranes which line the alveoli during the acute stages.

We wish to thank Professor J. B. Duguid for his interest and help in the study of the case.

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THE EYE IN INTRATHORACIC DISEASE

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The ocular complications of intrathoracic disease (excluding cardio-vascular disease) are not common, but when they do occur their recognition may be important. While in many cases there is an obvious association between an ocular and a chest lesion, the former may be insidious, resulting in severe local damage before adequate treatment can be given. On the other hand, the significance of a presenting eye condition may not be appreciated and the associated intrathoracic lesion overlooked. Whilst the most important connection occurs in tuberculosis and sarcoidosis, other diseases have manifestations in both areas. There are even associated congenital anomalies, as in neurofibromatosis, where tumours may be found in the orbit and in the thorax (Duke-Elder, 1945). Similarly in tuberous sclerosis, ocular phakomata may be seen in conjunction with the pulmonary forms of the disease, honeycomb lung and hamartomas (Dawson, 1954).

Acute Infections

Any acute infection may occasionally involve the uveal tract, leading to signs of iridocyclitis or choroiditis. Bacterial emboli from intrathoracic suppuration or pneumonia sometimes cause a purulent inflammation of the eye, but such a sequence is now becoming a rarity following the early use of antibiotics. Two specific infections which cause both a bronchiolitis and eye complications are measles and pertussis. The former causes a superficial keratoconjunctivitis usually with no sequelæ, but secondary infection may supervene and result in corneal ulceration and scarring. In pertussis, hæmorrhages may be caused by severe coughing. They may be found subconjunctivally, in the anterior chamber as a hyphæma or in the retina. They seldom cause permanent damage and require no treatment except rest in bed.

Neoplasms

Ocular symptoms and signs sometimes lead to the discovery of intrathoracic growths; for instance, thymomas associated with myasthenia gravis which may cause intermittent double vision or ptosis. Other intrathoracic growths may occasionally be diagnosed subsequent to ocular complications. A recent case has illustrated how the significance of a Horner's syndrome caused by a bronchial carcinoma was overlooked for nearly a year.

Although an examination of the eye is rarely of value in the early diagnosis of intrathoracic neoplasms, ocular changes may occur later. For instance, the eye shares in the congestion found in superior mediastinal obstruction from either a carcinoma or malignant reticulosis. Sometimes cerebral metastases cause papillœdema or oculomotor paralyses, but at this stage other signs are

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usually evident. Metastases may occur in the choroid, causing visual disturbances or signs of secondary glaucoma; an intra-ocular mass may be seen. Whenever an ocular neoplasm is suspected, a chest radiograph should be taken. This will exclude both a primary site in the lung and secondary deposits from an ocular melanoma.

Tuberculosis

Historical

Manz in 1858 confirmed histologically the earlier clinical descriptions of choroidal tuberculosis. Later, Cohnheim (1867) demonstrated that in miliary tuberculosis the choroidal nodules were identical with tubercles elsewhere in the body and that the condition could be reproduced in the guinea-pig by the inoculation of tuberculous material.

Primary Tuberculosis

The conjunctiva and its draining pre-auricular lymph nodes may be the site of a primary tuberculous complex, presumably caused by droplet infection (Fig. 1). This may spread locally into the eye or by the blood stream to the lungs. Primary ocular tuberculosis is rare, but primary infection in the lung or elsewhere may cause phlyctenular disease. This is a condition mainly affecting children and is relatively uncommon after the age of 20 years. Symptoms may be slight unless there is a complicating mucopurulent conjunctivitis or corneal involvement, when photophobia and lachrymation are often intense. The phlyctenule is a small pinkish-white elevation often situated near the corneo-scleral junction with an associated leash of dilated conjunctival vessels. If the cornea is affected, nodules appear in the superficial layers followed by connective-tissue formation and deep and superficial vascularisation. Corneal scarring may eventually be severe. The phlyctenule consists of an exudation of polymorphonuclear and mononuclear leucocytes into the deeper layers of the conjunctiva. It may resolve, but more often sloughs and heals by granulation. The tubercle bacillus is not found in the phlycten, and experimental inoculation of the organism into the conjunctiva is followed by a tuberculous reaction and not a phlycten. Although the individual conjunctival phlycten heals readily, recurrences are the rule. The treatment of corneal lesions is that for corneal ulcers generally—viz., the affected eye should be protected and the iris and ciliary body immobilised by atropine. In all cases, active primary infection should be sought and treated appropriately.

The Significance of Phlyctenular Disease

An assessment of the significance of phlyctenular disease as an indication of tuberculous infection is of great importance. Localised reactions of the phlycten type may be found against a background of specific bacterial conjunctivitis. Most phlyctenular disease does, however, constitute a clear-cut clinical entity, and there is much evidence to suggest that it is a manifestation not of local tuberculous disease but of a remote tuberculous focus, being somewhat akin to erythema nodosum. The phlycten only appears in a phase of high allergy in the presence of a local exciting factor.

The evidence pointing to tuberculous infection as the basis of the disease is

summarised by Sorsby (1942) and, though this has been vigorously disputed, in general the work of other observers supports the conclusions derived from his own large and carefully controlled series of cases followed over many years. His figures are given below as it is felt that they are more cogent than generalisations.

(1) Positive tuberculin reactions were found in 81·7 per cent. of a series of 230 children under 6 years of age with phlyctenular ophthalmia, whereas in a control group treated for blepharitis the incidence was 8 per cent. of 225 cases.

(2) Radiological evidence of intrathoracic tuberculosis was found in 72·2 per cent. of 510 cases. In the control group it was found in only 16·1 per cent. of 87 cases.

(3) Radiological evidence of active tuberculosis was found in 19·6 per cent. of 510 cases, whereas it was only found in 3·4 per cent. of a control group of 87 cases.

(4) The incidence of notified tuberculosis in a follow-up after an interval of between 6 and 16 years of 754 cases of phlyctenular disease was 5·3 per cent. with six deaths from this cause. Half the cases had tuberculosis of the chest. In a control group of 526 cases of blepharitis the incidence of subsequently notified cases was 0·9 per cent. and one patient had died from tuberculosis.

Thus phlyctenular ophthalmia indicates not only a high rate of active tuberculosis of the chest but an increased susceptibility later and a higher eventual mortality from this disease. It appears that in the majority of patients the phlycten is a manifestation of allergy following the invasion of the tubercle bacillus, though it must be recognised that in a small proportion of cases there is no evidence of tuberculous infection. These are probably due to allergy to other organisms.

Miliary Tuberculosis

The eye is commonly affected in disseminated miliary and meningeal tuberculosis by direct hæmatogenous infection. Characteristic tubercles are seen in the choroid (Fig. 2) and sometimes in the iris. They first appear as indefinite white patches later becoming more defined and associated with slight pigmentary disturbance. There may be some vitreous haze in their immediate neighbourhood.

Adult Type Tuberculosis

Ocular tuberculosis is seldom seen in patients with active post-primary or secondary tuberculosis, but is more common in healthy individuals with apparently inactive lesions. It is presumably due to an occasional bacillæmia.

Incidence of Ocular Tuberculosis in Patients with Pulmonary Tuberculosis

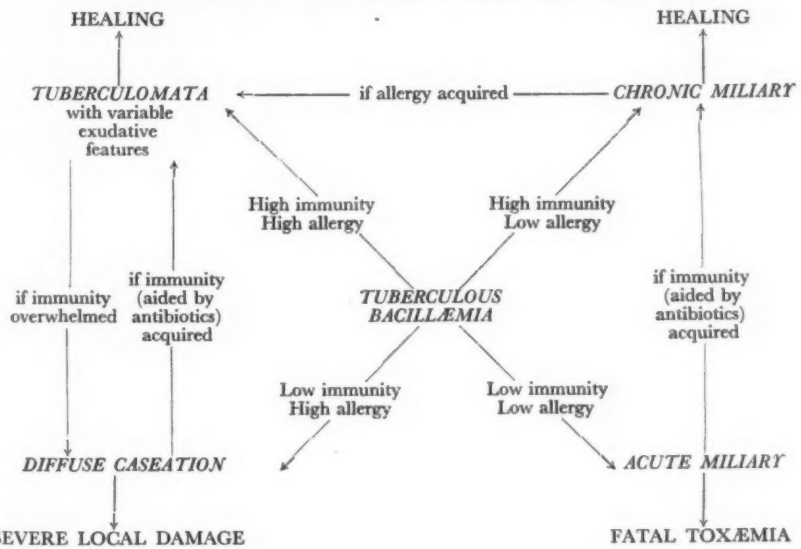
The importance given to this disease as a cause of endogenous ocular inflammation has varied widely in different places and at different times. Differing criteria for the diagnosis of ocular tuberculosis are largely responsible

and this invalidates figures purporting to give the incidence of the condition. It is exceedingly uncommon in sanatorium patients with pulmonary tuberculosis. Woods (1951) reports the incidence of manifest ocular involvement as less than 0·1 per cent. of 104,000 such patients. In 914 cases examined in detail by ophthalmologists, however, the incidence was 2 per cent. (Goldenberg and Fabricant, 1930).

Evidence of Systemic Tuberculosis in Cases diagnosed as Ocular Tuberculosis

Many studies have been made to locate the primary focus by clinical and radiological examination of patients diagnosed as having ocular tuberculosis. The value of these studies depends on the criteria adopted for such a diagnosis and the figures vary considerably. Thus Werdenberg (1935) in 500 cases found clinically detectable pulmonary tuberculosis in 10 per cent. and X-ray evidence of heavy hilar shadows but without clinical signs in 30 per cent. Grönholm (1928) found evidence of hilar gland disease in 55 per cent and of pulmonary infection in 18 per cent. of 100 cases, though no statement regarding activity was made, while X-ray examination of 80 patients by Woods (1938) revealed signs of tuberculosis in only 28 per cent.

THE POSSIBLE PATHOGENESIS OF OCULAR TUBERCULOSIS



The value of skin tests as an indication of the tuberculous nature of ocular inflammation has been disputed. Thus, Woods (1938) found positive Mantoux reactions at 1 : 100,000 dilution O.T. in only 53·4 per cent. of 180 cases of presumed ocular tuberculosis. Friedenwald and Dessoff (1935) found that only 6 out of 10 cases of histologically proved ocular tubercle reacted positively to 0·1 ml. of 1 : 100,000 O.T., while of 36 histologically non-tuberculous cases 5 gave positive reactions to the same test. It has been shown experimentally that in systemically infected animals, skin tests give a fairly reliable

indication of the ocular sensitivity to tuberculo protein (Woods, Burky and Friedenwald, 1938). These workers also showed that ocular tuberculosis with a high local sensitivity was compatible with a low skin sensitivity. This has been confirmed clinically while, conversely, positive skin tests may well be coincidental with non-tuberculous eye disease. However, when taken in conjunction with clinical features and after exclusion of other ætiological factors a positive reaction to 1 : 100,000 dilution is some evidence in favour of the tuberculous nature of an eye lesion.

The type of response to a tuberculous bacillæmia in the eye as in other tissues depends on the number and virulence of the infecting bacilli, the allergy of the tissues and the immunity of the patient. Thus, in the iris and choroid the lesion may vary from an exudative iridocyclitis or a diffuse granulomatous uveitis to the formation of tuberculomata which may remain discrete or may spread rapidly and coalesce with the destruction of the eye. The manner in which the various factors operate may be as indicated in the diagram.

Tuberculosis of the Iris, Ciliary Body and Choroid

The patient with an exudative iritis or cyclitis usually complains of aching and watering of the eye. Ciliary injection is found and is due to hyperæmia near the corneo-scleral junction, where perforating vessels pass through the sclera to the inflamed ciliary body and iris. The dilated capillaries of the uveal tissue allow the passage of abnormal amounts of protein and leucocytes into the aqueous humour. The protein shows as a cloudiness of the fluid in the anterior chamber and clumps of leucocytes may be seen on the posterior surface of the cornea comprising keratic precipitates or K.P. If the exciting agent causes a granulomatous response, nodules may be seen on the iris. In choroiditis the eye may appear normal externally, the condition only giving rise to visual symptoms. With the ophthalmoscope a pale œdematous area may be seen in the fundus through a hazy vitreous. Although the lesions are often single, they may be multiple, giving the picture of disseminated choroido-retinitis, a non-specific fundus appearance. Goldenberg and Fabricant (1930) in their careful survey of 914 proved tuberculous sanatorium patients did not see a single active tubercle of the eye, but pathological changes in the choroid and retina of a fairly constant pattern were found in 19 cases. They thought that the following changes indicated a healed tuberculous lesion:

(*a*) Comparatively normal blood vessels in the presence of marked choroido-retinal changes.
(*b*) White, yellowish or greyish spots surrounded by a fringe of pigment which appeared as if it were being slowly bleached out.
(*c*) Large diffuse areas of a light yellowish-pink or light grey in which pigment was irregularly distributed, and several well-defined pigmented spots slightly distant from the larger diffuse areas.

In iridocyclitis and choroiditis without specific clinical features often all that can be found histologically is non-specific infiltration and scarring, but, on the other hand, such conditions may prove to be tuberculous. Thus Woods (1938) carried out a histological examination of the eyes of seven patients with exudative iridocyclitis and found evidence of tuberculous inflammation and in

addition features of an acute allergic reaction. These findings have also been described by Verhoeff (1910, 1930).

Tuberculosis of the Retina

Retinal tuberculosis is usually caused by direct extension from choroidal tubercles, but may occur in the form of retinal periphlebitis. This was first described by Eales (1882) as " Primary Retinal Hæmorrhage in Young Men ". Its probable tuberculous origin has been deduced from the presence of active tuberculosis elsewhere in the eye (Axenfeld and Stock, 1911), and the presence of bacilli in the neighbourhood of the inflamed vein (Gilbert, 1935). The condition has also been reproduced experimentally by the systemic injection of tubercle bacilli. Clinically the vitreous hæmorrhage often obscures the retinal periphlebitis, but this may be visible ophthalmoscopically. Hæmorrhages are usually recurrent and when they cease there is either slow absorption or, more commonly, organisation in the vitreous, leading to retinal detachment. A disastrous secondary glaucoma may also supervene.

Tuberculosis of the Sclera

Tuberculosis is considered one of the most important causes of scleritis. If the anterior part of the sclera is affected, a chronic purplish-red, brawny congestion can be seen deep to the conjunctiva. When healed, a porcelain-like scar is left which may become ectatic. In more posterior lesions Tenon's capsule is involved and in these cases some degree of proptosis and immobility of the eye with œdema of the lids may occur. Scleritis is always associated with inflammation of the underlying ciliary body or choroid. Episcleritis is a more superficial condition, being an allergic reaction in response to various allergens of which tuberculo-protein may be one.

Tuberculosis of the Cornea

This is secondary to tuberculosis elsewhere in the eye. It may occur as an extension of a patch of scleritis or may appear as an interstitial keratitis. In comparison with the syphilitic variety it is more insidious in onset, the corneal vascularisation is by superficial as well as deep vessels and the resultant scarring is heavier and more superficial. While syphilitic interstitial keratitis is almost always bilateral and involves all parts of the cornea, the tuberculous variety tends to be unilateral and sectorial.

Deep infiltrates of the cornea may be of tuberculous origin, but they give rise to difficulty in making an ætiological diagnosis and on healing usually leave heavy scarring.

The Treatment of Ocular Tuberculosis

With rare exceptions a tuberculous lesion of the eye originates from a focus elsewhere in the body and both the general and local aspects of treatment must be considered.

(1) Promotion of the general powers of resistance by rest, adequate diet, fresh air and freedom from strain is an essential background to all other forms of treatment and may, of course, be effective alone.

(2) It has been shown that the intra-ocular concentration of streptomycin after systemic administration reaches therapeutic levels (Sorsby, Ungar and Bailey, 1952), providing this is given intramuscularly in full dosage, together with adequate oral P.A.S. In cases of ocular tuberculosis the course of treatment should be continued for at least a period of eight weeks in the absence of vestibular or other complications. Local administration of streptomycin eye ointment, 100 mgm. per gm., is probably also of value in anterior lesions.

(3) Tuberculin injections have many advocates in the treatment of ocular tuberculosis (Woods and Randolph, 1937). The treatment aims to achieve and to maintain desensitisation to tuberculo protein, thus preventing allergic reactions from interfering with healing. It acts as an adjuvant and does not replace other treatment. The dosage must be kept well below that which will produce a focal reaction in the eye or a local reaction at the site of injection. Desensitisation should be maintained for a prolonged period of at least two years to prevent the return of tissue hypersensitivity. Great caution should be observed in advocating tuberculin treatment in the presence of active pulmonary disease.

(4) Local treatment of inflammation of the uveal tract includes mydriatics and heat.

(5) The role of local cortisone treatment in ocular tuberculosis has not yet been worked out. Experimentally Woods and Wood (1952) have shown that in immune-allergic rabbits the usual restrained fibrotic course of ocular tuberculous inflammation is changed after the withdrawal of local or systemic cortisone to a caseating destructive lesion. There is some clinical evidence to support this, though it may yet be shown that the concurrent administration of streptomycin and P.A.S. or other anti-tuberculous drugs prevents such phenomena. Until this has been demonstrated, cortisone should be avoided in cases of proved or suspected ocular tuberculosis.

Sarcoidosis

Although Schumacher (1909) was the first to describe iritis in a patient with cutaneous sarcoidosis, and Heerfordt (1909) described a syndrome comprising fever, uveitis, parotitis and cranial nerve palsies, it was not until 1936 that Bruins Slot recognised the association with pulmonary and other forms of sarcoidosis. During the last decade there has been increasing interest in the disease, but the frequency of eye involvement is still uncertain. Thus, Ricker and Clark (1949) found ocular disease in 8·7 per cent, Longcope and Freiman (1952) 27 per cent. and 64 per cent. in their two groups of patients.

In a series of 90 patients with predominantly pulmonary sarcoidosis under the care of Dr. Clifford Hoyle at King's College Hospital, 18 showed eye involvement, an incidence of 20 per cent. All had uveitis, 4 an associated parotitis and 2 developed severe secondary glaucoma. Episcleritis, retinal periphlebitis, conjunctival sarcoidosis and band-shaped keratitis were each seen on one occasion in separate patients. The frequency with which ocular involvement is found partly depends on the care of examination, a slit-lamp examination by an ophthalmologist being necessary to detect minimal disease. Such an examination was made in the majority of this series of patients.

FIG. 1.—Primary conjunctival tuberculosis. Granulation tissue visible on medial portion of lower lid. Preauricular lymph node was enlarged. Biopsy of conjunctiva showed typical tubercle follicles.

FIG. 2.—Choroidal tubercles in a patient with miliary tuberculosis. Following treatment with streptomycin and P.A.S., the smallest tubercle disappeared and the others became smaller and more circumscribed.

FIG. 3.—Nodular iritis in a patient with pulmonary sarcoidosis. Slit-lamp painting also shows white keratic precipitates and pigment deposits on the lens.

FIG. 4.—Sarcoidosis of the conjunctiva and skin. The follicles on the lower lid were translucent and pale grey in colour. (Case 3).

FIG. 5.—Conjunctival biopsy in sarcoidosis (Case 3) showing early necrosis in one follicle. Biopsy after systemic cortisone, streptomycin and P.A.S. showed non-specific inflammatory reaction only. H & E stain × 70.

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Some idea of the importance of sarcoidosis as a cause of uveitis can be gained from Woods and Guyton's analysis (1944) of 200 patients with severe uveitis. They found sarcoidosis, proved by biopsy, in 15, but they thought that the correct frequency would be about 3 per cent., as their 200 patients were selected for full investigation because of the severity of the uveitis.

The appearance of uveitis in sarcoidosis may be non-specific and indistinguishable from that that found in association with other diseases—for example, rheumatoid arthritis. In about half of the cases the typical nodular iritis occurs which is usually painless and associated with minimal signs of inflammation (Fig. 3). The nodules are larger, pinker and more irregular than those seen in miliary tuberculosis, and frequently heal without a scar (Woods, 1951). Whilst the condition usually resolves with the aid of mydriatics, there may be a rapid deterioration with the development of secondary glaucoma or phthisis bulbi. The following case history illustrates this point.

Case 1, a 21-year-old man, noticed misty vision on leaving a cinema one night. This persisted and became worse during the succeeding ten days, when he was admitted to hospital. His visual acuity was found to be reduced to counting fingers at one foot and he had a severe bilateral iridocyclitis. The condition proceeded to gross destruction of the iris in both eyes with an organised hæmorrhagic mass in the vitreous. In the right eye a secondary glaucoma supervened with staphyloma formation within four weeks. Chest radiograph showed bilateral hilar node enlargement with lung infiltration in the right lower zone. The Mantoux was negative at 1 : 100 dilution, gastric washings were repeatedly negative for *M. tuberculosis* and liver biopsy showed typical epithelioid cell granulomata. Although the active inflammation in the eyes gradually subsided after treatment with mydriatics and systemic streptomycin, the vision of each eye was reduced to the perception of light.

When the lachrymal glands are enlarged in sarcoidosis there is usually an associated uveitis, this being one type of Mikulicz's syndrome. The changes found in the choroid and retina in sarcoidosis may be indistinguishable from those seen in tuberculosis, creamy-white nodules and retinal periphlebitis being the typical appearances. The choroidal nodules may leave irregularly pigmented scars on healing. Where corneal disease occurs, this is usually secondary to uveitis or sometimes associated with hypercalcæmia (Walsh and Howard, 1947). An illustration of the development of the typical band keratitis from deposition of calcium salts is given by the following patient:

Case 2, a 20-year-old man, was found to have enlarged hilar lymph nodes following a miniature radiograph in August 1952. Sputum cultures grew no M.Tb., the Mantoux was positive but only at 1 : 100 dilution of O.T., and liver biopsy showed typical epithelioid cell granulomata. Two months later he developed uveitis and retinal periphlebitis in the left eye, with generalised glandular enlargement. The inflammation subsided during systemic cortisone treatment, but the glands were little affected. A year later proteinuria was noticed, which was found to be due to renal stones. The serum calcium was consistently high. A few months later, at a time when the serum calcium was 14·7 mgm./100 ml., he noticed aching in the eyes and photophobia. He was found to have follicles on the exposed area of bulbar conjunctiva, each containing granular chalky material, and a band-shaped opacity in the cornea.

Further investigation of his calcium metabolism is now being undertaken, and treatment will be directed towards lowering the serum calcium level.

The following case history illustrates how iritis may be the first evidence of sarcoidosis. The patient also exhibited an unusual conjunctival form of the disease and showed a favourable response to systemic cortisone, streptomycin and P.A.S.

Case 3, a 62-year-old woman, developed non-specific iridocyclitis in the right eye in March 1951 which responded after a protracted course to local measures. No signs of disease elsewhere were found. Six months later she noticed redness and aching in the left eye. She was found to have an indurated mass beneath the lower tarsal conjunctiva with numerous follicles on the surface (Fig. 4). There were numerous enlarged lymph nodes, in the pre-auricular, occipital and cervical groups, and several typical skin lesions. Biopsy of the conjunctiva, skin and nodes showed characteristic epithelioid cell follicles, with early necrosis in one conjunctival follicle (Fig. 5). Chest X-ray revealed a fine reticular pattern throughout with enlarged hilar nodes. Culture and guinea-pig inoculation of biopsy material from all areas and sputum were negative for tubercle bacilli, Mantoux 1 : 1,000 positive. There was only slight improvement with local cortisone injections and systemic streptomycin and P.A.S. All the lesions then responded well when local cortisone was replaced by systemic cortisone starting with 150 mgm. daily for two months followed by a maintenance dose of 75 mgm. daily. A further conjunctival biopsy showed scarring and non-specific inflammatory tissue only.

It will be seen that many of the manifestations of ocular sarcoidosis have no characteristic features. The correct diagnosis may be suspected if a nodular iritis is seen, but confirmation should be sought by a thorough clinical examination for skin lesions, lymph node or splenic enlargement. A chest radiograph may reveal enlarged hilar nodes or lung infiltration, in which case sputum or gastric washings should be examined to exclude tuberculosis. The Mantoux test is frequently, though not invariably, negative. The most secure foundation for a diagnosis of sarcoidosis rests on biopsy of skin, lymph nodes or liver.

Treatment

Many examples of uveitis in sarcoidosis are mild and heal spontaneously with the aid of mydriatics. When the inflammation is severe, cataract, secondary glaucoma or phthisis bulbi may develop with severe impairment of vision. These complications were found in 10 of 43 cases with eye involvement in the literature (Levitt, 1941) and in 2 of the 18 patients at this hospital. In an attempt to prevent these disasters, cortisone and ACTH have been used by many ophthalmologists to suppress the inflammation in severe or extensive forms of ocular sarcoidosis. Anterior uveitis has been shown to respond to topical cortisone or subconjunctival injections (Ainslie and James, 1953), but when there is no response, and in more posterior lesions, systemic treatment is required (Shulman and others, 1952). This may need to be continued for some months. If the disease is then quiescent, improvement can sometimes be maintained by local treatment. There is undoubtedly a close relationship between sarcoidosis and tuberculosis, and cortisone by inhibiting granulation tissue and immune responses may precipitate active tuberculosis (Lovelock and Stone, 1953). For this reason we advocate systemic streptomycin and P.A.S. or isoniazid whenever ACTH or cortisone is used in treating sarcoidosis.

Summary

A review of the ocular associations of intrathoracic disease shows that their recognition is of value to the chest physician. The typical appearances of ocular tuberculosis are described. The significance of phlyctenular ophthalmia in relation to primary tuberculosis is discussed. A description is given of the ocular lesions of sarcoidosis which occur in about 20 per cent. of cases. The treatment of ocular tuberculosis and sarcoidosis is outlined.

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TUBERCULOSIS OF THE UPPER AIR PASSAGES AND EARS

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During the past forty years the mortality from tuberculosis has fallen consistently and this downward progress was only slightly interrupted by the two world wars. The annual number of deaths now is only a third of the 1913 figures. The total number of cases of tuberculosis reported has not undergone the same reduction, but the morbidity is greatly diminished. Morbidity figures include tuberculous lesions of the larynx, pharynx, mouth and ears.

Forty years ago between 20 and 30 per cent. of all tuberculous patients developed tuberculous lesions in the larynx and perhaps 1 per cent. developed lesions in the pharynx, the mouth or the ears. Today the laryngeal lesions occur only in 2-3 per cent. of cases and the other lesions are now only occasionally seen.

It is not easy to point to any one particular reason for this reduction, for there are probably a number of contributory factors. There may have been a change in the virulence of the causative organism. Such fluctuation is known in other bacterial diseases—scarlet fever and measles being two examples. These changes may be brought about by persistent and partly successful treatment when bacteria are being bred from strains whose virulence has been diminished by such treatment. Possibly, the virulence of the organism has not changed, but a nation-wide resistance has developed; a resistance that is shared by many of the more highly developed nations but not by the undeveloped ones. This resistance may be at least in part due to the improved standard of living and nutrition during the period under review. Working hours and conditions have improved, but for much of the population there is still gross overcrowding in old and insanitary buildings, and this factor is responsible for the high level of new cases of tuberculosis.

Other factors that have helped in the reduction of both mortality and morbidity are earlier diagnosis and more efficient care and treatment. The introduction of tuberculosis dispensaries and chest clinics and the appointment of special tuberculosis medical officers have played a great part in the new developments. Mass radiography has also helped to discover early cases at a treatable stage.

Apart from artificial pneumothorax no real improvement was introduced in the treatment of phthisis until the advent of plastic operations on the thoracic cage and paralysis of the diaphragm in the third decade of the century.

The introduction by Waksman in 1944 of streptomycin was one of the most notable advances in the treatment of tuberculosis and has had a profound

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effect on the outlook for patients with tuberculous lesions in the upper air passages. It used to be considered that the existence of a tuberculous lesion in the larynx reduced the patient's chance of survival by half, and the presence of such a lesion in the pharynx or mouth meant death within three to 12 months. The menace to life of tuberculosis in the nose and ear was not so immediate, but the disease was very obstinate and treatment might include operative measures.

The patients with ulcerative lesions in the phrarynx and larynx suffered extreme pain on swallowing, so that severe cases suffered from considerable degrees of starvation. This pain was difficult to combat, requiring constant medication before each meal, and blocking measures were applied to the sensory nerve concerned.

The use of streptomycin has altered the course of tuberculous lesions in the upper air passages more than in any other region. Whether in the ear, nose, pharynx, mouth or larynx a comparatively short course of streptomycin brings about complete disappearance of the infection. The more active and acute the lesion the more quickly and the more completely does the lesion disappear, and only in the occasional case, even where the general and pulmonary condition are seriously deteriorating, does it recur. Streptomycin acts most quickly and surely on the active tubercle and on the growing edge of an ulcer. The pain usually arises at this site and, the effect of streptomycin is to dissipate the pain for good in three or four days. There is not very much obvious change in the appearance of the ulcer at this stage, but after a two to three weeks' course of 1 gramme of streptomycin daily the ulcer is obviously healing or the tuberculous infiltration shrinking, and after 30 to 60 grammes have been given the lesion is usually quite healed. The occasional case may require 90 to 100 grammes—usually a non-ulcerative type of case. The sodium salt of para-amino salicylic acid is always given—8 grammes three times a day—to prevent the bacilli from becoming resistant to streptomycin.

The chronic long-standing infiltration is slowest to disappear and there may always be a certain degree of thickening of the mucous membrane, although the disease seems to be completely destroyed.

In the ear a lesion of the mucous membrane involving the middle ear cleft and the mastoid antrum will clear up equally well, and it is found that, even if there is a secondary pyogenic infection, the otitis clears up. The organisms in a chronic otitis media are usually Gram-negative and sensitive to streptomycin, but occasionally a Gram-positive streptococcus or staphylococcus may be present and penicillin or aureomycin may be required to clear up this secondary infection. If the bone of the mastoid process is severely involved a radical mastoidectomy may be necessary to promote healing.

When streptomycin was first used in the treatment of tuberculosis, doses of 3 grammes a day were followed by perceptive deafness and by vertigo. Reduction of the daily dose to 2 grammes abolished the deafness, but the vertigo continued. Administration of 1 gramme a day reduced the incidence of vertigo to a small proportion, and this symptom was often only transitory. One gramme of streptomycin a day is sufficient to clear up the great majority of upper respiratory lesions. Tests of the vestibular system showed permanent damage to that system where the higher doses had been given, but with 1 gramme daily

the damage was often not complete and the system recovered after the cessation of treatment. Doses of less than 1 gramme daily have been used—usually 1 gramme every third day—but it has been found that this is barely adequate to resolve the lesions of the throat and mouth, and certainly requires a much longer time to effect a recovery.

A new compound, dihydrostreptomycin, was prepared by reducing streptomycin and was claimed not to harm the vestibular system but to be as powerful, if not more so, in the treatment of the pulmonary disease. It is true that this compound is relatively innocuous to the vestibular system, but it has a serious toxic effect on the acoustic system, producing a severe perceptive deafness which is usually irreversible. This deafness tends to appear at the end of a course of treatment or even after its termination and to be progressive for some time. The drug has not been demonstrably superior in its effects on the pulmonary disease and there seems no justification for its further use.

Much work has been carried out in attempts to locate the site of the damage to the acoustic and vestibular systems. The results of the various observations point to the end organ in both systems as the affected part, damage only being caused to neural elements when amounts many times larger than any possible therapeutic dose have been administered.

Tuberculous meningitis has become a curable disease since the advent of streptomycin, and of the considerable number of individuals who have survived a proportion are found to be deaf. The deafness is of a perceptive type, and is progressive for some weeks or months after the cessation of treatment. It is rarely total but nearly half the patients were so severely deaf as to be classified as sub-totally deaf. It was thought at first that the deafness was an example of streptomycin toxicity, but the histological examination of a number of temporal bones from such cases has demonstrated that tuberculous infiltration of both parts of the eighth nerve is fairly common and that damage to either the cochlear or vestibular end-organs is rare. This suggests that such deafness may be due to implication of the acoustic nerve in the meningeal tuberculosis. A similar phenomenon occurs in meningococcal meningitis, and presumably after the disappearance of the tuberculous infiltration of the nerve enough scarring takes place to cause the deafness found in survivors.

Confirmation of these views is contained in the work of Gunnar Lidén, who has found that the recruitment phenomenon is present in patients who have become deaf following administration of the antibiotics in question—demonstrating the end-organs as being the site of the lesion. He found no recruitment in those patients who had survived tuberculous meningitis and who were deaf, demonstrating that the site of the lesion was in the nerve.

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THE HOLST TYPE THORACOPLASTY

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When upper thoracoplasties are performed for pulmonary tuberculosis with cavitation about 10 per cent. of cases are found to have residual cavitation.

The late Professor Holst (1952) investigated a hundred such cases referred to his clinic and, while resecting the diseased lungs, was able to examine the chest wall. He concluded that re-expansion of the apex was the crux of the problem and found that it occurred no less in cases in which apicolysis had been performed than where no strip was done.

Many diverse procedures have been employed to prevent this re-expansion; principally the gauze plug, air refills of the apicolysis space, oil or wax plombs, polythene pads, bone chips, dextrose saline infusions and resected ribs.

In a paper on the subject Holst discusses these methods and goes on to describe his dome thoracoplasty, which utilises the ribs and intercostal bundles as a new osseo-muscular roof, maintaining the collapse obtained by apicolysis.

In this paper we review fifty-four Holst-type thoracoplasties performed by members of the Newcastle Regional Thoracic Surgical Service between May 1951 (Mason performed the first operation at Poole Hospital, Middlesbrough) and August 1953.

The Operation

The operation is performed under general anæsthesia with the patient in the lateral position. The incision and approach to the ribs is as for a classical thoracoplasty. The roof is fashioned from the first four or five bundles together with the second, third and fourth ribs, or the third and fourth ribs, or the third, fourth and fifth ribs, depending on the extent of the disease. In this series the first rib was retained in twenty-one cases (cleared subperiosteally on its lower surface). The second rib was retained in four cases, being utilised as part of the roof in three. The posterior half of the fifth or sixth rib is cleared subperiosteally on its inner surface. The bony portion of the roof is formed by removing the posterior ends of the ribs from the neck to the angle and in front by removing about an inch so that each rib is slightly longer than the rib above. Apicolysis is then performed. In most cases in this series this was done extrapleurally. During the strip the bundles are divided posteriorly and the first two bundles anteriorly. The roof is then fixed in place, the posterior ends of the second and third bundles are sutured together to the spinal ligament at the level of the fourth thoracic vertebra. The fourth and fifth bundles are fixed more laterally and at a lower level. Anteriorly the first and second bundles are sutured together to the lateral edge of the sternum at the level of the

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second interspace. The free ends of the ribs are fixed laterally and at lower levels. The first bundle is then sutured to mediastinal fat to prevent herniation of the apex. The lowest bundle used for the roof is fixed to the intercostal space below by means of three mattress sutures to pull the roof taut and prevent paradoxical respiration. All patients receive blood during the operation.

TABLE I.—AGE INCIDENCE OF HOLST TYPE THORACOPLASTIES

	15-19 *yrs.*	20-24 *yrs.*	25-29 *yrs.*	*Over* 30
Males	2	7	4	12
Females	7	12	3	7

Total 54

INDICATIONS

Our patients have been selected principally from cases in which thoracoplasty was indicated for unilateral upper lobe disease although, later in the series, cases were used where bilateral collapse appeared necessary.

Because we considered the post-operative shock of the Holst-type thoracoplasty to be greater than that of the conventional two-stage operation we restricted its use to our fitter, and therefore normally younger, patients.

Holst also performed the operation for cavitation in the apical segment of the lower lobe, but no such case occurs in our series. The operation was limited to cases in which the apical disease extended no farther than the sixth rib posteriorly on a postero-anterior film, less extensive disease requiring correspondingly less collapse.

PRE-OPERATIVE RÉGIME

All patients in this series had undergone treatment in various hospitals and sanatoria. Most of them had had courses of chemotherapy and bed-rest and occasionally artificial collapse therapy had been tried and had failed. In some cases the lesion was quiescent; in others cavitation persisted and no further improvement was taking place with conservative measures.

Patients undergoing the operation were prepared beforehand both physically and mentally for the procedure. Respiratory function tests were performed on all cases, the doubtful ones having maximum breathing capacity and differential bronchospirometry. The blood picture was checked and breathing exercises commenced.

POST-OPERATIVE RÉGIME

In the immediate post-operative phase the patient is nursed with the foot of the bed raised. The blood pressure, pulse and respiratory rates and colour are charted at half-hourly intervals and oxygen is given to all cases.

The blood drip is continued for as long as necessary and, as the condition improves, the patient is raised to a sitting position.

Coughing is encouraged when the patient has fully recovered conscious-

FIG. 1.—Left upper lobe cavitation.

FIG. 2.—After upper thoracoplasty (Holst Type).

FIG. 3.—Right upper lobe cavitation.

FIG. 4.—After upper thoracoplasty (Holst Type).

FIG. 5.—Showing apical re-expansion after two-stage thoracoplasty.

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ness. After twenty-four hours, arm and breathing exercises are commenced and X-rays are taken in bed with a portable machine.

TABLE 2.—MAJOR COMPLICATIONS

	No.	*Deaths*	*Paradoxical Respiration*	*Atelectasis*	*Effus.*	*Space Infection*
5 Rib	27	1	2	9	7	1
6 Rib	27	–	2	14	9	1

COMPLICATIONS

Pleural tears with associated hæmo-pneumothorax and atelectasis are the most common complications of the operation. They occurred in twenty-seven cases in our series and were treated by adequate aspiration as soon as possible. These tears were not always accidental at the time of operation, some developing up to two days afterwards. This may be due to the pleura tearing on the rib ends. Immediate tears are most likely to occur when clearing the under surface of the fifth and sixth ribs, particularly when the pleura is abnormally thin. Of twenty-one of our cases where artificial pneumothorax had been attempted previously, nine developed this complication, the resultant blood in the pleural space causing prolonged post-operative pyrexia.

Tears occurring during the operation should be closed immediately if possible. When this cannot be done, or when a large tear has been closed, an intercostal drain should be inserted, connected to an underwater seal and left in place until the lung has fully expanded. Many clinics do this in all cases of pleural tear. After aspiration of air and fluid the lung usually expands quite rapidly, bronchoscopies being only very occasionally required.

PARADOXICAL RESPIRATION

This particular complication is rare, occurring in only four cases in our series. The patients were firmly padded and oxygen administered.

With the fixed roof, paradoxical breathing should not occur. Holst discovered, by using metal clips to indicate the position of the roof and sutures, that it was caused by the failure of the fixation sutures to hold the roof in place. This was confirmed in our cases, two of which also developed anoxæmia with pulmonary œdema necessitating frequent bronchoscopies. X-rays showed apical re-expansion above the original roof level, again evidence that the fixation sutures had failed.

LARGE EFFUSION INTO SPACE ABOVE THE DOME

Increase in effusion above the dome caused distress by pressure; increase in strip and prolonged post-operative pyrexia took place in thirteen cases. Amounts of up to 40 ounces of blood-stained fluid were aspirated. Increased experience of the operation and more meticulous hæmostasis have now almost eliminated this complication.

Spread and Reactivation

A spread or reactivation of tuberculosis occurred in five cases.

In one the spread took place in the immediate post-operative phase and, as it involved the whole of the homo-lateral lung, a pneumonectomy was performed.

In two cases cavitation persisted under the Holst roof. In one the sputum became positive two years after operation, X-rays showing active disease in the opposite side as well. In the remaining one the persisting cavity was closed by a "second stage" operation. The fifth and sixth ribs and a part of the roof fourth rib were removed with cavity closure and sputum conversion. In the remaining two cases there was reactivation and an increase in disease in the contra-lateral lung some six months after operation.

Infection

Staphylococcus aureus infection occurred in two cases in the space above the dome. This was treated by thoracotomy and cleaning out of necrotic tissue and pus from the space, closing the wound and giving large doses of active antibiotics. After prolonged convalescence both wounds healed satisfactorily.

Mortality

One case, a girl in the 15-20 age group, died a few hours after operation. Her death was confirmed at post-mortem to be due to myocardial failure associated with shock. In retrospect it appears that she was not in a good enough general condition to undergo the operation despite seven months' bed rest and six months' chemotherapy.

Discussion

The two-stage thoracoplasty has proved its value for more than a quarter of a century, but it has certain disadvantages, some of which are eliminated by the Holst-type operation.

The Holst thoracoplasty is performed in one stage, post-operative paradoxical respiration is diminished, mutilation is negligible and arm function is unimpaired. Re-expansion is prevented by the presence of a fixed roof, the diseased area being covered by bone or bone-forming tissue. It is a mechanically sounder procedure, the necessary collapse being obtained and maintained more easily.

Being a one-stage operation it causes less apprehension and obviously shortens the stay of the patient in the surgical ward, thereby increasing the turnover.

The sputum conversion rate is high in our series, two cases remaining positive, one with a persistent cavity under the dome and the other with spreading disease at the other apex. In his larger series, Holst was able to claim 90 per cent. conversion. These advantages, in our opinion, outweigh the disadvantages of longer operating time, greater post-operative shock and greater liability to pleural tear, all of which will no doubt be reduced by further experience.

Patients in sanatoria who take great interest in the treatment of their condition are usually pleased to hear that a Holst-type "plasty" has been advised in their case. Some even ask if one could be performed instead of the two-stage operation.

TABLE 3.—FOLLOW-UP OF FIFTY-THREE CASES

Time since Operation	*Disease*		*Working*	
	Active Pos.	*Quiescent Neg.*	*Yes*	*No*
24-32 months	2	23	21	4
18-23 months		11	10	1
12-17 months		9	4	5
6-11 months		8	2	6

Total 53

Fifty-three cases were followed up for a period varying from six to thirty-two months. Of these, the disease is quiescent and sputum negative in 51. Of 36 followed up for a period of eighteen months or more, 31 are well, leading a normal life and working. Of the remaining 5, 2 have active disease, the other 3 show no evidence of active disease.*

Apart from the 2 cases in which there has been reactivation (in one case under the dome, in the other at the contra-lateral apex), no patient has experienced any permanent complications arising from the operation or from the disease.

Summary

Fifty-four cases of one-stage dome thoracoplasty performed for apical tuberculosis are reviewed. The technique of the operation is briefly described, the indications and post-operative complications are discussed. A follow-up of from six to thirty-two months is presented. In spite of the high immediate complication rate which will decrease, it is hoped, with increasing experience, the operation is of great value and is an improvement on the two-stage operation in that the apex after apicolysis is held down by a fixed dome.

Our thanks are due to Mr. G. A. Mason, F.R.C.S., Senior Surgeon, Newcastle-upon-Tyne Regional Thoracic Surgical Service, for his encouragement; to Dr. R. Cunningham, Physician Superintendent, Poole Hospital; to Dr. J. P. Parkinson, Physician Superintendent, Holywood Hall Hospital; and to the area Chest Physicians for their co-operation in the follow-up investigation.

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* Of the 17 followed up for a period of six to eighteen months, 6 are back at work and 11 are either doing light work or have not yet returned to work.

SPONTANEOUS PNEUMOTHORAX COMPLICATING PNEUMOPERITONEUM THERAPY

By Gwyn Howells

From the Derby Chest Clinic

Spontaneous pneumothorax is a well-recognised but unusual complication of pneumoperitoneum therapy. No case of a unilateral left-sided pneumothorax has previously been reported as a complication. Smith (1943) described a bilateral, fatal pneumothorax which occurred after the induction of a pneumoperitoneum. Apart from this, all other cases have been on the right side only.

The three cases described below have two particular features of interest. Two of them are the first recorded cases of left-sided pneumothorax in pneumoperitoneum therapy, and the three together represent rather an unusual incidence, as all occurred in the same chest clinic within a period of four months.

Case Reports

Case 1. V.W., a woman aged 25 years, was first seen in December 1949 when, following a mass radiograph, she was found to have pulmonary tuberculosis with infiltration and cavitation in both upper zones. Her sputum contained tubercle bacilli.

She was admitted to the Derwent Hospital on 15.3.50, after a period of three months' bed rest at home during which time she had a course of streptomycin 1 G. combined with P.A.S. 15 G. daily for thirty days. During her stay in hospital she was kept on rest and given two courses of streptomycin 1 G. with P.A.S. 18 G. daily for thirty days. She also had a four-months' period of postural retention for the left lung cavity. A pneumoperitoneum was induced in March 1951 and resulted in satisfactory rise of the diaphragm. Fills were done on the left side 2 inches below the costal margin. No phrenic crush was performed. When discharged to continue rest at home on 8.7.51, her general condition was much improved but her disease was still active; bilateral cavitation was still visible in the X-ray and her sputum remained positive.

For the next twenty-six months her pneumoperitoneum was maintained uneventfully. Her general condition and her disease deteriorated slightly: her sputum remained positive.

On 9.9.53 she had a normal refill, after screening, of 1,000 c.c. of air. The pressures were +12 before and +13 +15 after refill. About four hours later she had a moderate fit of coughing after climbing some stairs. During the coughing she felt a pain in her right chest and shortly afterwards became dyspnœic. She was seen by her general practitioner, who diagnosed a pneumothorax and admitted her to the Derwent Hospital. X-rays showed a right pneumothorax with the lung held out by numerous adhesions and a small pool of fluid in the costo-phrenic angle. A large tension cavity was visible at the right apex. The pneumoperitoneum was still present but was not so large as might have been expected on the day after her refill.

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Her recovery from the pneumothorax was uneventful, and by 5.10.53 the lung had re-expanded. Her present condition is now much as it was prior to this incident.

Case 2. C.B., a man aged 34 years, was first seen in August 1951, when he gave a history of cough with copious sputum over the preceding three months. He was found to have advanced bilateral pulmonary tuberculosis with infiltration in all zones, a large cavity at the left apex and a small one on the right. He was toxic and his general condition was poor. Sputum was positive for tubercle bacilli.

He was admitted to the Derwent Hospital on 25.8.51 and was discharged 21.5.53. During this time he was kept at rest and had altogether 78 G. of streptomycin and 80 G. of I.N.H. Both the streptomycin and I.N.H. were accompanied by 18 G. of P.A.S. daily and the bacilli remained sensitive to all three drugs. The small cavity in the right lung closed, but the large cavity in the left apex remained unaltered. He was tried on a five-months' period of postural retention, but, although this considerably diminished the size of the cavity, it did not close it. By March 1953 his general condition had greatly improved; the X-ray appearances were much better; there was no obvious toxæmia and only occasional sputum, but this remained positive. During March a left phrenic crush was performed, followed, a fortnight later, by the induction of a pneumoperitoneum. This resulted in a satisfactory rise of the left diaphragm, but it was noted that the inner half of the right diaphragm was abnormally thin. The pneumoperitoneum further diminished the size of the cavity, but the latter remained open and the sputum positive.

The prognosis was thought to be poor and the most to be hoped for was the achievement of " good chronic " status. Following his discharge the pneumoperitoneum was satisfactorily maintained over the next five months. Refills were given on the left, 2 inches below the costal margin. Clinical improvement was maintained and the radiological appearances remained unaltered.

On October 9 he was given his normal fill of 1,000 c.c. after X-ray screening. Pressures were +2 before and +5 +7 after refill. Some two hours after his fill he had a severe bout of coughing which left a slight discomfort. This slowly worsened through the night and the following day, when he also became dyspnœic. He was readmitted to the Derwent Hospital on 11.10.53 and was found to have a left pneumothorax. X-ray showed almost complete collapse of the lung except at the left apex, which was bound down by adhesions and where the cavity remained visible and " suspended." There was a small puddle of fluid in the left costo-phrenic angle. The pneumoperitoneum was present, but the amount of air was not as large as might have been expected. Under-water drainage of the air was instituted after 700 c.c. had been removed (pressures before and after removal, 0+5 and −5−1). His immediate condition improved, but the fluid increased steadily, and on 23.10.53 30 oz. of clear straw-coloured fluid, in which tubercle bacilli were found, were removed. Treatment had previously been commenced with streptomycin 1 G. and P.A.S. 20 G. daily, and streptomycin was now given into the pleural cavity after aspirations. Subsequent progress has been steady, with slow re-expansion of the lung and diminution in the fluid, but he remains under treatment for tuberculous empyema.

Case 3. E.J., a man aged 35 years, was first seen in June 1951, having had a small hæmoptysis. He gave a history of severe asthma and bronchitis since infancy. In childhood he had had tuberculous spinal disease from which he had made a good recovery but which had left a marked kyphosis. More

recently he had had a duodenal ulcer. He was found to be suffering from advanced bilateral pulmonary tuberculosis with cavitation in both upper zones. His sputum contained tubercle bacilli.

Treatment was commenced at home with bed rest and a course of streptomycin 1 G. with P.A.S. 15 G. daily. On 7.7.51 he was admitted to the Derwent Hospital, where he stayed until 21.5.53. During this period he was treated by rest, streptomycin to a total of 56 G. combined with P.A.S., and in March 1953 he had a right phrenic crush followed by the induction of a pneumoperitoneum. On discharge there had been improvement in his general condition and in the X-ray appearances, but his sputum remained positive and cavitation was still visible in the apices. At this time he was up for two hours daily and his most troublesome symptom was dyspnœa on slight exertion.

His pneumoperitoneum was maintained without difficulty for the next five months at the chest clinic. Refills were given 3 inches below the right costal margin. During this time his general condition deteriorated steadily, although his tuberculosis showed only slight alteration. His asthma and bronchitis, which had troubled him little while in hospital, returned, and by November he was dyspnœic even on the slight exertion of walking. He had marked signs of chronic bronchitis and his heart showed signs of strain. The pneumoperitoneum was maintained, although the ultimate prognosis was hopeless, mainly because the patient attained considerable relief of his dyspnœa after each refill.

On 23.12.53 he was screened prior to his refill and the pneumoperitoneum was noted to be rather shallow, but no new abnormality was seen in the lung fields. On commencement of the refill the pressure was +12 (usual range for him being between +8 and +15) and the air flowed easily. After about 300 c.c. of air, he complained of a pain in the left chest and a sense of fullness in the chest; the refill was discontinued. About three or four minutes later dyspnœa had become distressing, and the patient developed acute pulmonary œdema with marked physical signs and copious thin, frothy, pink sputum. The pulse became rapid and almost impalpable, cyanosis deepened and he lost consciousness during the attack. He was treated with morphia gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{100}$ and continuous oxygen therapy. This resulted in considerable improvement and he was transferred to the Derwent Hospital. There, the pulmonary œdema having subsided, he was found to have clinical signs of a left pneumothorax. 350 c.c. of air were withdrawn from this with further improvement in his condition. X-ray after this showed a small left-sided pneumothorax. Some air was present under the diaphragm, but the state of the pneumoperitoneum could not be accurately adjudged as, owing to his general condition, the X-ray was taken with the patient lying on a stretcher. Consciousness was regained but his general condition remained poor, and later, during the evening, he had a further attack of dyspnœa, collapsed and died. No post-mortem examination was obtained.

Commentary and Discussion

All three cases had bilateral advanced lesions. Phrenic crush had been performed in two of the patients; in one it was on the same side as the subsequent pneumothorax. All previous reports confirm that diaphragmatic paralysis plays no part in the occurrence or site of pneumothorax, where it complicates pneumoperitoneum. The first two patients ascribed the onset of their symptoms to attacks of coughing. Some form of incident (coughing, defæcation, sudden

bending, etc.) that results in a sudden increase of intra-abdominal pressure has been described in over a third of the reported cases. The incidence of this precipitating factor may well be higher, as in several reports the information is not available.

In Case 2 there was a notable thinning of the inner half of the right diaphragm, but the subsequent pneumothorax occurred on the left. Apart from this no radiological abnormalities of the diaphragm were seen in the series. No diaphragmatic blebs were seen as in the case of Yannitelli *et al.* (1949), but no tomography was done.

It is interesting to note the marked relief of dyspnœa experienced by Case 3 after his refills. In fact, when it was at one time suggested that the pneumoperitoneum might be abandoned, he was insistent that it should be maintained because of the easing of his breathing. Pneumoperitoneum has, of course, been used as a treatment of emphysema (Reich, 1924; Furman and Callaway, 1950) and in asthma with or without bronchitis (Rubin and Gass, 1948).

Two other cases with fatal issue have been described (Smith, 1943; Yannitelli *et al.*, 1949). The cause of death in the third case is a matter for conjecture, and in this connection it is regrettable that no post-mortem examination could be obtained. There appear to be three possible causes. The symptoms are those that might be expected with an air embolism, and Simmonds (1946) describes a very similar case, where at necropsy there had been evidence of trauma of the liver, by which the air was thought to have reached the heart. In his case the fill had been a difficult one, necessitating two attempts, and the air had run very slowly. Symptoms came on after 150 c.c. had been introduced and death occurred in a minute or so. The objections to this diagnosis in Case 3 are: the fill appeared a normal one, the air ran quickly and easily, there was an interval of at least three or four minutes before dyspnœa commenced, and lastly, it does not account for the pneumothorax. The second possibility is that the pneumothorax was the primary cause of death in so far as it occurred suddenly in a man who was already at the limit of his respiratory reserve. The pneumothorax, although small, might then have precipitated the acute pulmonary œdema. Here it might be objected that the symptoms were too acute in onset and considerable improvement in his condition had already taken place before air was removed from the pleura. The last possibility is that death was due to mediastinal emphysema. The concept of this complication of pneumoperitoneum therapy is set out by Simmonds (1946). It is suggested that air from the peritoneum might pass into the mediastinum beside the œsophagus and aorta. From the mediastinum it may spread to give interstitial emphysema of the lungs, or, in other directions, to give rise to subcutaneous emphysema of the neck, or a pneumothorax. The symptoms produced by mediastinal emphysema, as described by Macklin and Macklin (1944), are due to compression of the veins in the lung roots and may closely resemble air embolism. The diagnosis of mediastinal emphysema would seem to account for all the symptoms of Case 3, including the pneumothorax.

Spencer Jones and Yuill (1952) point out that two types of case exist. The pneumothoraces, which develop immediately after the induction of a pneumoperitoneum, are due to congenital diaphragmatic defects. Those which develop later in the course of the maintenance of the pneumoperitoneum appear

to be traumatic in origin. For the cause of the latter group two main theories have been advanced. The theory of mediastinal emphysema has been presented by Banyai and Jurgens (1940) and Simmonds (1946). Other authors, notably Spencer Jones and Yuill (1952), have supported the theory of a traumatic tear in the diaphragm as the cause of the bulk, if not all, of the cases. The evidence, which has been recently summarised by Johnson (1953), would appear to be strongly in favour of the occurrence of diaphragmatic rupture. The main objection to mediastinal emphysema as a cause is that it does not account for the great preponderance of right-sided pneumothoraces. Dickie (1948) showed that, when pneumothorax complicates mediastinal emphysema, both sides are equally affected. Although it does not account for the majority, there seems to be no reason why it should not be the cause of the occasional case such as the third patient described above.

The factor of coincidence also merits consideration. Spontaneous pneumothorax may occur as an unusual complication of active pulmonary tuberculosis, quite apart from pneumoperitoneum therapy. When it occurs in active tuberculosis, it is very likely to be followed by infection of the pleural space with tubercle bacilli. It seems reasonable that on rare occasions it might be met with as a coincident but unrelated event in tuberculous patients who have a pneumoperitoneum. This must be considered as a possible explanation for Case 2, who rapidly developed an infected pleura after the onset of his pneumothorax.

Summary

Three cases of spontaneous pneumothorax occurring in the course of pneumoperitoneum therapy are described.

Two of the pneumothoraces occurred on the left side and are the first recorded cases.

Mediastinal emphysema is advanced as the explanation of one of the left-sided cases.

All three cases occurred within a period of four months.

I would like to thank Dr. H. G. Grace and Dr. R. J. O. Taylor for their permission to publish these cases and for their helpful criticism.

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PULMONARY TUBERCULOSIS AND THROMBOCYTOPENIC PURPURA

REPORT OF A CASE

By John Balint*

From the Brompton Hospital, London

Idiopathic thrombocytopenic purpura is an uncommon disease, especially in men. Its association with pulmonary tuberculosis is even rarer, for recently Ellman and Johnson (1952) could find only eleven examples reported in the literature. The following report gives details of a further case:

Case Report

F.M., a chef, aged 44 years, was first seen on March 24, 1953. For four days he had been coughing blood-stained sputum and had had a red rash. He also admitted to a cough and night sweats for about a year, in which time he had lost 2 stone in weight.

On admission to hospital he was seen to be an ill man. He had marked clubbing of the fingers, but was afebrile and had a normal rate of pulse and respiration. He weighed 10 stone 12 pounds. There was a widespread purpuric eruption over the trunk, limbs, face and buccal mucosa. Macroscopic hæmaturia was present.

There were signs of consolidation at the apex of the right lung. The heart was normal. Neither spleen nor liver was palpable and there were no enlarged lymphatic nodes.

Investigations

His E.S.R. was 22 mm./hr. (Westergren); Hb. 98 per cent. (14.5 gm./100 c.c.), W.B.C. 9,000, polymorphs 73 per cent., eosinophils 2 per cent., lymphocytes 18 per cent., monocytes 7 per cent.; *Platelets:* 28,000/c.mm.; *Bleeding time:* (Dukes) over 30 min.; *Prothrombin time:* 10 secs. (control 10 secs.).; and *Coagulation time:* (Dale and Laidlaw) 2½ mins. *A chest radiograph* on 24.3.53 showed a contracted right upper lobe and diffuse mottling over both lung fields, with probable cavitation in the right mid zone. *Tomography* on 7.4.53 confirmed the presence of cavitation. *Sputum* did not show any tubercle bacilli on concentration in two specimens.

Course

The bleeding time gradually diminished from the time of admission. In view of the radiological findings, treatment with streptomycin 1 gm. daily and I.N.A.H. 100 mgm. b.d. was started on 2.4.53. On 28.3.53 platelets were 48,000/c.mm. and the bleeding time 3½ mins. On 8.4.53 platelets were 35,000 and bleeding time 4 mins. On 7.4.53 tubercle bacilli were found in the sputum by concentration, and their presence was subsequently repeatedly confirmed by culture. His general condition improved rapidly; by 9.4.53 the bleeding tendency had stopped. On 15.4.53, therefore, it was considered safe

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to carry out a sternal puncture. This showed a moderately hyperplastic marrow, containing numerous rounded megakaryocytes with vacuolated cytoplasm. There was virtually no evidence of maturation of platelets. The appearances were considered typical of idiopathic thrombocytpenic purpura.

Further improvement was made with a gain in weight.

By 21.4.53 the platelets had risen to 61,000 (Hb. 98 per cent.) and by 2.5.53 the platelets were 136,000/c.mm. By 12.5.53 the platelets had risen further to 206,000/c.mm. and the bleeding time now was 1¼ mins (Dukes). Further marrow puncture was done on 14.5.53. The marrow was now less active than a month previously, with fewer megakaryocytes which were more nearly normal than previously.

At the present time the patient is well, having gained over 1 stone in weight His sputum still contains scanty tubercle bacilli but the volume of sputum has decreased. A blood count on 1.7.53 showed Hb. 101 per cent., W.B.C.'s 8,000, normal differential count, platelets 183,000/c.mm. His E.S.R. was 10 mm./1 hr. Radiologically there has been a decrease in the size of the cavity in the right mid-zone, but otherwise no significant change. He has now had a two-stage right thoracoplasty without a further hæmorrhagic incident.*

Discussion

Thrombocytopenic purpura may be idiopathic, commonly called primary, or secondary to a principal disease or to drugs given for its treatment or the relief of its symptoms. The increased numbers of chemotherapeutic agents has led to drug purpuras becoming commoner than the primary form. Their recognition is important as appropriate treatment will greatly help the patient.

Purpura in association with tuberculosis has been noted from time to time for more than 150 years. Willan in his *Treatise on Cutaneous Diseases* (1801) noted purple spots which occurred as the heralds of death in pulmonary tuberculosis. Thrombocytopenic purpura has been recorded as secondary to tuberculosis affecting the spleen or bone marrow (Winternitz, 1912), or widespread tuberculous infection affecting the peritoneum as well as other parts (Hoyle and Vaizey, 1937), but isvery rare—probably rarer than the equivalent condition of leucopenia associated with tuberculous septicæmia (Ball, Joules and Pagel, 1951). Both are found almost exclusively in widely disseminated tuberculosis without evidence of host resistance and have hitherto proved generally rapidly fatal. Ellman and Johnson (1952) recently reported a case of their own and gave a very full review of the literature.

Recently Stefani and Dameshek (1953) confirmed that platelets are antigenic. They suggested that " it is conceivable, although not demonstrated, that bacterial and viral agents and other noxious agents may modify the structure of the platelet and confer on it auto-antigenic properties." This would correspond to auto-immune hæmolytic anæmia, a well-recognised, though rare, condition. Moreover, acute thrombocytopenic purpura is frequently preceded by infection or drug administration. In this case pulmonary tuberculosis was almost certainly present for some considerable time before the onset of the purpura. Ackroyd (1949 a) in studying three cases of thrombocytopenic purpura due to sedormid (allyl-isopropyl acetylcarbamide) showed that

* Since this report was written this patient has gone to Sanatorium. He is up all day and his sputum is now negative for tubercle bacilli.

application of sedormid to the skin of a sensitised subject resulted in a localised purpuric eruption without a fall in the platelet count, and was, therefore, presumably due to capillary damage. He further demonstrated (1949 b and c) that sedormid produced a substance in sensitised subjects, which causes agglutination and lysis of platelets. These findings support the above hypothesis of Stefani and Dameshek (1953).

Purpura following intradermal injection of old tuberculin has been recorded on three occasions (Wright and Boccal, 1923; Gonzalez Batlle, 1941). These cases were not associated with thrombocytopenia and may correspond with the type of reaction produced by local application of sedormid to sensitised subjects (Ackroyd, 1949 a).

As thrombocytopenic purpura tends to spontaneous recovery or remission it is hard to say whether the treatment, in this case, of the tuberculous infection had any effect on the blood disorder. Secondary purpura due to drugs may confidently be excluded here, as no treatment had been given until after the development of purpura. Nor was there any clinical evidence of extra pulmonary tuberculosis. Furthermore, recovery from the thrombocytopenic purpura started before the commencement of anti-tuberculous treatment, and proceeded at the usual pace for this condition. It seeems likely, therefore, that this patient suffered from a chance coincidence of thrombocytopenic purpura and pulmonary tuberculosis. That this may be so for all reported instances is suggested by the fact that Ellman and Johnson (1952) in their review of the literature could find only thirty-eight cases of pulmonary tuberculosis and purpura, and that only eleven of these were thrombocytopenic. Considering the vast number of patients suffering from pulmonary tuberculosis, now and in the past, a greater incidence than this might be expected, were pulmonary tuberculosis the cause of thrombocytopenic purpura.

In conclusion it may be said that the case for a causal relationship between pulmonary tuberculosis and thrombocytopenic purpura is not proven, though such a relationship may exist.

Summary

A case of pulmonary tuberculosis and thrombocytopenic purpura is reported and the association is discussed. A causal relationship is not yet proven.

I wish to thank Dr. Howard Nicholson for permission to record this patient who was under his care and also Dr. S. W. A. Kuper for the marrow and hæmatological studies.

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TUBERCULIN SENSITIVITY AND TUBERCULOSIS IN 1,779 NURSES

By Graham Poole*

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Since the Queen Elizabeth Hospital was opened in 1939 all nursing students entering the preliminary training school have been Mantoux tested and X-rayed. Further X-rays were taken at three-monthly intervals and vigorous efforts were made to repeat the Mantoux test until conversion took place. From April 1950, B.C.G. was offered to all negative entrants while still in the preliminary training school. Following discussions with Dr. Brian Taylor, it was decided that interesting results might well repay an investigation of the tuberculin sensitivity of entrants, subsequent changes in sensitivity in negative reactors and an examination of the incidence of tuberculosis among the nurses. It was hoped that examination of the initial tuberculin sensitivity would provide figures which could be compared with other surveys—notably the Prophit Survey and the M.R.C. National Tuberculin Survey. The occurrence of tuberculosis among nurses in a teaching hospital, its effect upon training and cost, would be revealed by the investigation. The effect of previous occupation upon tuberculin sensitivity, Mantoux conversion and attendant phenomena were also problems which could be examined. Further, facts could be ascertained which might, in the future, enable one to determine the value of B.C.G. in the same hospital.

Nurses accepted for training were all educated to School Certificate standard; the majority were recruited from the Midlands, though substantial numbers came from other parts of England and Wales and a few from elsewhere (Ireland, Scotland, the Commonwealth and Europe). The Queen Elizabeth Hospital is a general hospital, but about ten known cases of pulmonary tuberculosis have regularly been under treatment in the hospital, so that in this respect the hospital falls between the Group A and Group B hospitals of the Prophit Survey.

It was recognised that many deficiencies would limit the value of the results —for example, several resident medical officers, during the period 1939-52, had been responsible for Mantoux testing, the three monthly re-testing sometimes fell behind schedule, and from the beginning of 1946 to the end of 1949 only 0·1 c.c. of 1/1,000 old tuberculin was used.

Initial Tuberculin Reaction

Old tuberculin was used throughout—at some periods three strengths (0·1 c.c. of 1/10,000 (0·01 mgm.), 0·1 c.c. of 1/1,000 (0·1 mgm.) and 0·1 c.c. of 1/100 (1·0 mgm.)); at others only two strengths; while between 1946 and 1949 only 0·1 mgm. old tuberculin was used. It is, therefore, possible through-

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out to compare the sensitivity to 0·1 mgm. old tuberculin. The reaction was read at 72 hours and œdema of more than 5 mm. diameter was read as positive.

The records of 1,779 nurses have been examined. Of these, 1,653, between April 1939 and October 1952, had been admitted to the preliminary training school; an additional 126 records were those of "second year" nurses, who had already completed two years' training elsewhere. Of 1,653 nurses tested with 0·1 mgm. old tuberculin, 986 (59·7 per cent.) were positive and 667 (40·3 per cent.) negative; of the 667 negative, 145 were positive to 1·0 mgm., so that to 0·1 mgm. and 1·0 mgm. together 68·4 per cent. were positive.

Table I shows the initial reaction to 0·1 mgm. old tuberculin and to 0·1 mgm. and 1·0 mgm. combined in various age groups.

TABLE I

Age	*Number*	*No. Positive to 0·1 mgm.*	*% Positive*	*No. Positive to 0·1 mgm. and 1·0 mgm.*	*% Positive to both*
18	1,020	581	57·0	667	65·4
19	262	167	63·7	187	71·4
20	116	77	66·4	87	75·0
21	56	37	66·1	44	78·6
22	33	21	63·6	23	69·7
23	21	14	66·7	15	71·4
24	15	10	66·7	14	93·3
25 and over	65	51	78·5	52	80·0

Table II shows the initial reaction of new entrants year by year of all age groups together and of the ages 18 years, 19 years and 20 years and over. In the first column, sensitivity is shown of all age groups to 0·1 mgm. and 1·0 mgm. combined; in the other columns, sensitivity is shown to 0·1 mgm. only.

TABLE II

Year	*All ages combined*			*All ages*			*Age 18*			*Age 19*			*Age 20 and over*		
	No. of entrants	*Pos. 0·1 and 1·0 mgm.*	*% Pos.*	*No. of entrants*	*Pos. 0·1 mgm.*	*% Pos.*	*No. of entrants*	*Pos. 0·1 mgm.*	*% Pos.*	*No. of entrants*	*Pos. 0·1 mgm.*	*% Pos.*	*No. of entrants*	*Pos. 0·1 mgm.*	*% Pos.*
1939	91	72	85·7	91	69	75·8	27	18	66·7	19	15	78·9	44	38	86·4
1940	94	77	81·9	94	67	71·3	49	34	69·4	18	13	72·2	26	20	76·9
1941	66	53	80·3	66	35	53·0	35	18	51·4	11	4	36·4	16	12	75·0
1942	65	53	81·5	65	38	58·5	29	15	51·7	15	10	66·7	16	11	68·7
1943	110	90	81·8	110	75	68·2	57	37	67·3	11	8	72·7	38	27	71·1
1944	111	98	88·3	111	82	73·9	51	38	74·4	34	25	73·5	19	14	73·7
1945	116	90	77·6	116	85	73·3	71	52	71·8	29	21	72·4	16	12	75·0
1946	Only 0·1 mgm. O.T. used			106	43	40·6	68	28	41·2	22	10	45·5	15	5	33·3
1947				159	96	60·4	109	63	57·8	22	15	68·2	28	19	67·9
1948				149	83	55·6	112	63	56·3	17	9	52·9	16	11	68·7
1949				142	73	51·4	101	48	47·5	16	9	56·3	16	10	62·5
1950	149	99	66·4	149	91	61·1	83	49	56·9	20	15	75·0	18	10	55·6
1951	146	97	66·4	146	76	50·7	103	50	48·5	18	11	61·1	17	7	41·2
1952	149	101	67·8	149	75	50·3	125	68	54·4	10	2	20·0	13	5	38·5

Table I shows a steady rise in sensitivity from the age of 18 to 25 and over, while Table II shows that there has been a fall in sensitivity between 1939 and 1952. It is interesting to compare the present figures with those given in the Prophit Survey—the model in this field. 5,085 nurses were tested (1934-39), 80·2 per cent. were tuberculin positive with which the figures in Table II for 1939-43 show close agreement. In relation to age, the Prophit figures show that at 18-19 years 80·6 per cent. were positive, rising to 86·7 per cent. at 24 years and over.

The Medical Research Council's National Tuberculin Survey of 1949-50 showed the following results for females: aged 17-18, 47·8 per cent. to 61·1 per cent. positive; aged 19-20, 55·7 per cent. to 73·2 per cent. positive. The lower percentage in each case is for urban England south of Rugby and the higher percentage for urban England (north and midland) and Wales. Table III shows the figures obtained in some other surveys.

TABLE III

Author	*Year*	*Country*	*No. of persons*	% *Tuberculin positive*
Edwards *et al.* ..	1945	England	148 (nurses)	80·0
Israel *et al.*	1941	U.S.A.	643 (nurses)	57·0
Grimes *et al.*	1947	Ireland	3,337 (city girls)	69·0
Rich	1951	U.S.A.	Average of 20 surveys in U.S.A. since 1930	(age 15-20) 42·7 (age 20-25) 60·0
Thompson	1949	New Zealand	503 (nurses)	50·5
Annotation in *Tubercle*, p. 237, Vol. XXIX	1948	France	Students entering French Universities	46-73

THE EFFECT OF PREVIOUS OCCUPATION ON TUBERCULIN SENSITIVITY

The effect of previous occupation on the tuberculin sensitivity is compared in Table IV with entrants having no previous occupation. In the third section of this table the sensitivity is recorded of girls with some previous nursing

TABLE IV

Age	*No. prev. occ.*	*No. Pos. 0·1 O.T.*	% *Pos.*	*Some prev. occ.*	*No. Pos. 0·1 O.T.*	% *Pos.*	*Previous nursing experience*	*No. Pos. 0·1 O.T.*	% *Pos.*	*Second-year nurses*	*No. Pos. 0·1 O.T.*	% *Pos.*
18-19	450	271	60·2	474	288	60·75	223	128	57·4	12	7	58·3
20-21	35	24	68·6	115	80	69·6	58	41	70·7	48	24	50·0
22-23	11	7	63·6	35	23	65·7	16	14	87·5	47	40	85·1
24 and over	12	9	75·0	50	35	70·0	26	20	76·9	19	19	100·0
All ages tog.	508	311	61·2	674	427	63·6	329	203	61·7	126	90	71·4

experience, which usually implies a period of some months as an assistant nurse in a variety of hospitals while waiting to commence training. In the fourth

section, second-year nurses are those who have previously trained in another special hospital (orthopædic, children's, etc.) for a period of two years. The second section, nurses with some previous occupation, includes those with previous nursing experience (section three), but not second-year nurses (section four).

Except in the case of second-year nurses the percentage of positive reactions is very similar. Thus it would seem that neither a short period of previous nursing nor other occupation increases the percentage of positive reactors entering the preliminary training school as compared with girls having no previous occupation. It appears, on the other hand, that a higher proportion of positive reactors can be expected from girls who have already had two years' recognised training. The Prophit Survey revealed no significant difference between groups with and without previous occupation.

Mantoux Conversion during Training

Nurses admitted to the preliminary training school remain under observation for four years, some longer, and every effort was made to repeat the Mantoux test (0·1 mgm.) at three-monthly intervals. Some nurses gave up training and some of the records of re-testing are incomplete. Of 314 nurses negative on entering and with complete records, 229 or 72·9 per cent. converted to positive. (From April 1950 all non-reactors to 1·0 mgm. were given B.C.G.) Conversion, in 229 nurses, occurred at an average of 13·5 months from the commencement of training.

The Prophit Survey nurses showed a conversion rate of 78·3 per cent. in the first year of training (Daniels). Other observers have given conversion rates, over a period of three years, from 58 per cent. (Pollack and Cohen) to 85·7 per cent. (Amberson and Riggins). Thompson in New Zealand found that over a period of five years only 72 (28·9 per cent.) of 249 nurses Mantoux negative on entry converted during training.

Ten cases of erythema nodosum occurred. In six nurses, negative on entry, erythema nodosum occurred within a few months of conversion; the longest period was nine months, while in three of these cases known to be negative three months earlier, the first positive Mantoux was recorded at the onset of erythema nodosum. The nurse who developed erythema nodosum nine months after conversion had a primary lung lesion at the same time and three years later developed an active lesion in the same part of the lung. One nurse, whose conversion was noted at the same time as her erythema nodosum, developed first a left pleural effusion after two months, then a right-sided effusion after a further seven months and subsequently pulmonary tuberculosis. In two cases, positive on entry, erythema nodosum occurred within a few months of entry, but the relationship to conversion is not therefore known. Erythema nodosum also occurred in three nurses positive on entry at seventeen, twenty and thirty months respectively after entry. Certainly in the last three cases and possibly in five of the cases, erythema nodosum may well have occurred as a hypersensitive manifestation to a condition other than tuberculosis. In one of the cases, positive on entry, erythema nodosum occurred seventeen months after and, within eleven months of this, a pleural effusion developed suggesting that

erythema nodosum may have occurred in relation to tuberculosis long after the primary infection. Except in the three cases of erythema nodosum developing further lesions, and described above, the X-ray appearances remained normal during and after erythema nodosum.

One case of phlyctenular conjunctivitis occurred certainly within three months of conversion.

Four cases with constitutional symptoms and radiological evidence of hilar gland enlargement occurred within two or three months of conversion and two cases of " dry " pleurisy with pyrexia within three months of conversion.

Daniels (1944) in 285 conversions reported five cases of erythema nodosum, fourteen cases with " symptoms referable to the chest " and no case of phlyctenular conjunctivitis.

Morbidity

Table V shows details of cases of tuberculosis arising after entry to training.

Table V

Type of case	*Initial Mantoux reaction*		*Total*
	Negative	*Positive*	
Active pulmonary tuberculosis	9	6	15
Subclinical pulmonary tuberculosis	2	2	4
Pleural effusion	8	6	14
Pleurisy without effusion	2	0	2
Primary complex with symptoms	3	1	4
Non-pulmonary tuberculosis	1	0	1
	25	15	40

In addition to the forty cases included in Table V, four showed pulmonary lesions, thought to be inactive, when the nurses were admitted to the training school; one of these subsequently became active, requiring treatment. A fifth nurse, known to have had peritonitis (tuberculous) and a pleural effusion before training, developed pulmonary tuberculosis. One nurse died of tuberculous meningitis (the non-pulmonary case in Table V).

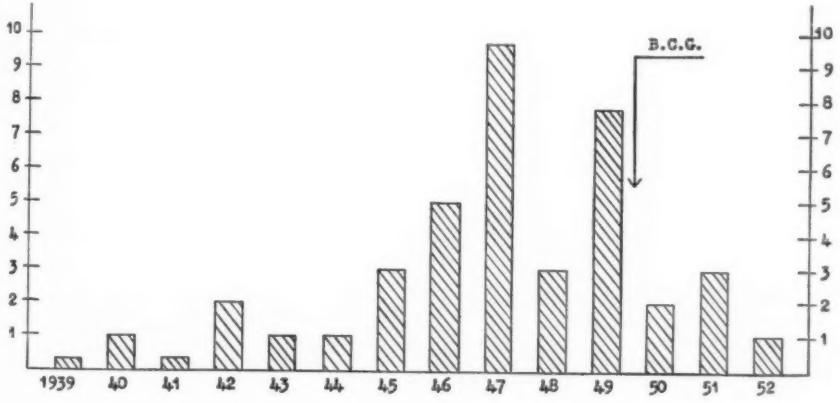
The morbidity in relation to the year of training showed little difference when comparing the initially negative and positive cases. Excluding the primary lesions the average length in months from entry to discovery of the lesion was twenty-three in negative cases and twenty-two in positive cases. Of more significance, however, in the twenty-five nurses negative initially is the interval between conversion and the development of the lesion. The average length of this interval was eight months, in twelve of the cases it was under six months, which strongly suggests that the twelve to eighteen months following conversion are particularly dangerous. The Prophit Scholars found that the case rate in nurses tuberculin-positive on entry was 0·7 per cent. in the first year after entry, whereas the rate is 10·4 per cent. in the first year after Mantoux conversion.

The total of forty cases gives a case incidence of 2·2 per cent. in 1,779 nurses observed for three to four years on an average. The figures given in the Prophit

Survey are for 2,774 Group B nurses 1·80 per cent. and for 1,286 Group A nurses 1·94 per cent. (these figures exclude Irish and Welsh nurses; the overall incidence is quoted as 2·3 per cent.). Other surveys of over 1,000 nurses, quoted in the Prophit Survey, show an incidence of between 1·3 per cent. and 3·0 per cent.

The incidence in 558 nurses negative on entry was 4·5 per cent.; comparable figures in the Prophit Survey are 3·49 per cent. for Group B nurses and 3·87 per cent. for Group A nurses. The incidence in 1,221 nurses positive on entry was 1·2 per cent. compared with 1·27 per cent. for Group B nurses and 1·57 per cent. for Group A nurses. The figures from the Prophit Survey exclude Irish and Welsh nurses in each case.

The graph shows the distribution of cases referred to in Table V throughout the years 1939 to 1952. The B.C.G. programme was commenced in 1950. There has not been a new case of pulmonary tuberculosis since 1949. There is no certain explanation of the higher case incidence between 1947 and 1949, though it is interesting to note in this connection that the proportion of negative entrants (Table II) between 1946 and 1949 was high, especially compared with preceding years. This is true even though one may feel suspicious of the extremely high percentage of negatives during 1946. Thus with a larger group of negative reactors at risk a higher morbidity rate might be expected.



All the nurses referred to in Table V (except the fatal case of meningitis) returned to training mostly after breaks of about nine months, though some longer. Quite apart from the interruption of training and the anxiety of nurses and staff, such prolonged illnesses are clearly costly.

Conclusions

The enlightened plan, started when the hospital was opened in 1939, to X-ray and Mantoux test all entrants to the Queen Elizabeth Hospital, to re-X-ray at three-monthly intervals and re-test negative reactors at three-monthly intervals, was pressed home commendably well in spite of the difficulties of

the war years. The place of routine X-ray examination in those exposed to such an occupational hazard as tuberculosis is obvious and proved invaluable in detecting lesions early. Equally, the detection of conversion alerted the medical staff so that the increased risks of succeeding months were kept closely in mind. The increase in tuberculin sensitivity with age (Table I) and the reduction in sensitivity in recent years (Table II) accord with the findings of other surveys.

The effect of previous occupation on entrants' tuberculin sensitivity appears to be negligible, except in the case of girls who have had two years' recognised training as nurses elsewhere. This seems reasonable, since the latter group contains girls who have worked in, for example, children's hospitals, orthopædic hospitals, fever hospitals, where the risk of exposure to tuberculosis would be increased. On the other hand, most of the other previous occupations for the type of girl concerned would be temporary, light and relatively protected. In the case of girls with some previous nursing experience this would usually have been short and the contact with patients less.

The section on Mantoux conversion is incomplete because a small number of the records of re-testing are deficient and these cases are not included. The occurrence of erythema nodosum in six cases shortly after conversion serves to emphasise the well-known relationship, but the other cases of erythema nodosum also show that no particular relationship, to conversion at least, can be assumed.

The incidence of morbidity in the Mantoux-negative entrants is the striking feature of the section on morbidity and leads naturally to a consideration of how this might be reduced. At the centre of this problem are the Mantoux-negative nurses and their sources of infection. To take the sources of infection first, it is clear that undetected cases of pulmonary tuberculosis are the chief problem, both because no measures are taken to neutralise the unsuspected case and because Mantoux-negative nurses would not be directed to nurse known cases. Further evidence in support of this contention is that efforts to relate infection in nurses to known cases failed in all but one instance, and in this case a nurse shortly after the onset of her illness became engaged to a patient. Awareness of this danger has led to the frequent or routine use of chest X-rays for cases admitted to most of the wards.

The problem of the Mantoux-negative nurse is best tackled by protecting her with B.C.G. Consequently, since April 1950 all negative entrants have been offered B.C.G. and this had been accepted in all but two or three of 130 entrants by the end of 1952. One of the nurses given B.C.G. developed a pleural effusion but, by the end of 1953, it already seems that the morbidity is much reduced, to which end B.C.G. is surely contributory. More certain evidence will perhaps be forthcoming in a year or two. Dahlström and Difs state that between 1941 and 1944, 61,474 Swedish Army conscripts were tuberculin negative; 36,235 or 59 per cent. accepted B.C.G. After six months pleural effusion had occurred in 46 cases in the vaccinated group (1·27 per 1,000) and 145 in the un-vaccinated group (5·75 per 1,000).

It is suggested that the measures used at the Queen Elizabeth Hospital should be employed in all general hospitals.

Summary

The initial Mantoux reactions of 1,779 nursing entrants to the Queen Elizabeth Hospital, Birmingham, between 1939 and 1952 are analysed. At the age of eighteen 57·0 per cent. were positive to 0·1 mgm. old tuberculin, while at twenty-five and over 78·5 per cent. were positive. With all ages combined, over 70 per cent. were positive to 0·1 mgm. old tuberculin in 1939-40, but only 50 per cent. in 1951-52. The figures are compared with those obtained in other surveys, notably the Prophit Survey.

Previous occupation, compared with no previous occupation, does not appear to alter the proportion of positive entrants except in the case of nurses who have already completed a two year course of training in one of the special hospitals. Combining all ages, 61·2 per cent. with no previous occupation were positive to 0·1 mgm. old tuberculin, 63·6 per cent. with some previous occupation were positive and 71·4 per cent. of second-year nurses were positive.

Complete records of regular retesting were available for 314 nurses initially negative, 229 or 72·9 per cent. converted during training. Eleven cases of erythema nodosum occurred; of these, six developed within a few months of conversion, two developed soon after the commencement of training in initially positive nurses and three at intervals of seventeen, twenty and thirty months after entry in initially positive nurses. One case of phlyctenular conjunctivitis developed shortly after conversion.

Forty cases of tuberculosis arising during training are classified in Table V, twenty-five of them occurred in nurses initially Mantoux negative. The case incidence in negative entrants was 4·5 per cent., but only 1·2 per cent. in nurses initially positive.

Various aspects of these findings are discussed. In particular the danger of the twelve to eighteen months after conversion confirmed by this investigation, is stressed. B.C.G., which has been offered to all negative entrants since 1950, already seems to be proving helpful. Routine chest X-ray examination of patients admitted to hospital is desirable to eliminate the dangerous unsuspected sources of infection.

I wish to thank the Medical Advisory Committee of the Birmingham United Hospitals for permission to publish this article. I am greatly indebted to Miss B. Byrne for her kind, patient and generous help in extracting the details upon which the article is based. Dr. A. Brian Taylor inspired the investigation; both he and Dr. F. Ridehalgh have given most helpful advice for which I am most grateful.

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REVIEWS OF BOOKS

Tuberculosis in B.C.G. Vaccinated and Non-Vaccinated Young Adults. A comparative prognostic study. By GUNNAR DAHLSTROM. Copenhagen: Acta Tuberculosea Scandinavica, 1953. Supplement XXXII. Pp. 136. Price not stated.

In 1951 the author, in collaboration with the late Hans Difs, presented in Supplement XXVII of the Acta Tuberculosea Scandinavica an investigation into the efficacy of B.C.G. vaccination. This is referred to in some detail in the present communication, which is supplementary to it. It covered the years 1947-51, when 174,966 Swedish army recruits were tuberculin-tested and 61,474 (35·1 per cent.) were found not to react to 1 mg. of tuberculin. 36,235 (58·9 per cent.) of these non-reactors were vaccinated with B.C.G. vaccine and 25,239 (41·1 per cent.) were not. The two groups were comparable in age and in the distribution of areas from which they were enlisted, and were the material of both investigations. 167 (0·46 per cent.) of the vaccinated and 345 (1·25 per cent.) of the non-vaccinated developed some form of tuberculosis. The difference was statistically significant for all types of the disease—primary tuberculosis, tuberculous pleurisy, acute miliary tuberculosis and tuberculous meningitis, and the post-primary forms. One weak point of the investigation was that only 74 per cent. of those vaccinated had subsequent tuberculin tests, but that difficulty is dealt with statistically in both investigations.

The objects of the present investigation were (1) to find out whether B.C.G. vaccination influences the course of tuberculosis arising in vaccinated people, (2) to study the prognosis of tuberculosis developing in those who receive a primary infection in adult life, and (3) to study resistance to tuberculosis in areas of varying population density, the previous investigation having suggested that tuberculin-negative conscripts from sparsely populated areas in northern Sweden had on the average poorer resistance than those from densely populated areas in the central and southern parts of the country. Previous literature with a bearing on these and similar points is reviewed at length and in detail.

The results of the first part of the investigation are considered under the headings of primary tuberculosis, with which are grouped ocute miliary tuberculosis and tuberculous meningitis and exudative pleurisy; post-primary pulmonary tuberculosis; and other tuberculous disease such as tuberculosis of bones and joints, glands and genito-urinary tract. The rate of progression through the groups is analysed, as also are the five-year mortality figures. A point on which stress is laid is that the development of effective immunity against pleurisy and pulmonary tuberculosis after B.C.G. vaccination lags behind the appearance of allergy and is unlikely to be present within four to six months of vaccination. This is of obvious importance in assessing the results of vaccination. The results themselves are far from striking and are influenced, in the opinion of the author, by the 26 per cent. of the vaccinated group who were not tuberculin-tested. If this group is excluded there is a small balance in favour of the vaccinated. There was no evidence that those who could be assumed to have been infected immediately before vaccination, or before protection had developed, had a poorer prognosis than the controls.

It may seem irrelevant in such an investigation to devote a chapter to the prognosis of primary tuberculosis in adulthood as compared with childhood. Clinicians of experience have long been familiar with the dangers of infection in young adult life and the death figures confirm the vulnerability of this period. This chapter confirms what is to a large extent already known and the author maintains that his results justify vaccination of young tuberculin-negative adults. It must be remembered that his results deal with young males who, by virtue of acceptance for military service, were presumably healthy. The tuberculosis morbidity and mortality figures for all young women are probably much higher, and few will contest the author's plea in a later section for protective vaccination of the whole young adult group. His analysis of the prognosis of tuberculous exudative pleurisy should bring little comfort to those who consider this to be a benign condition.

In a recent communication to local authorities the Ministry of Health and the Department of Health for Scotland have sanctioned schemes for offering B.C.G. vaccination to children before they leave school. Children of 15 and over are to be excluded so as not to interfere with the Medical Research Council's current trial of B.C.G. in school-leavers. The Ministry states that there is as yet no scientific evidence of the true value of B.C.G. vaccination, and recognises that some authorities may prefer to wait until the results of these trials are available in three years' time before themselves launching new vaccination schemes. There is an air of detached complacency about this statement which must surprise Continental authorities. It accords ill with the present disquiet over morbidity figures. Others believe in the efficacy, albeit comparative, of B.C.G., and if in three years' time the vaccine has been discredited by the M.R.C. trials, or in the minds of the local authorities themselves, it can be abandoned. All believe that B.C.G. is harmless. The difficulties of maintaining the organism at a suitable level of virulence are fully realised, but the percentage of non-reactors in all series published in this country has been small and there is enough evidence in its favour to justify its more extensive use.

CHARLES CAMERON.

Tuberculosis in Childhood and Adolescence. With special reference to the pulmonary forms of the disease. By F. J. BENTLEY, S. GRZYBOWSKI and B. BENJAMIN. London: The National Association for the Prevention of Tuberculosis. 1954. Pp. xii+259. 67 illus. 30s.

That tuberculosis in childhood can take the form of severe pulmonary disease is within the experience of all physicians with special experience in chest disease, as well as pædiatricians. As Sir Robert Young points out in a preface to this book, the authors leave us in no doubt that childhood pulmonary tuberculosis can be just as varied in form, perplexing in diagnosis and as difficult to treat as the more familiar pulmonary tuberculosis of adults. The High Wood Survey covers 1,049 consecutive tuberculosis cases in childhood treated at High Wood Hospital, or discharged from or dying in, the hospital during the years 1942–46, and the survey was followed up during 1949–52.

Pulmonary tuberculosis in childhood falls into two main patterns:

(1) Primary tuberculous disease and its complications, which form the great majority of cases.

(2) Chronic pulmonary tuberculosis, akin to the common form in adults, which form a small minority of cases.

The conclusions reached will be generally accepted. It is recognised that primary infection is, in the main, uneventful and that the more localised lesions are, as a general rule, overcome, but the hæmatogenous miliary and meningeal lesions may prove fatal; the first two years of life constitute the most dangerous time at which infection can occur and the first year following infection is the period of greatest risk. The age of the child and the probable duration of infection are of far greater significance than the nature of X-ray shadows in the chest in the management of tuberculosis in childhood, although the complications of primary infection of blood-borne dissemination or miliary or meningeal disease are responsible for 90 per cent. of all deaths. Bronchogenic spread plays little part in the deaths from primary disease.

Chronic pulmonary tuberculosis in childhood (bronchogenic tuberculosis) is, however, a rare and graver disease, and the authors have analysed 116 such cases of whom approximately 80 per cent. were 13 years of age or more. The management and treatment of this type of lesion, in which antibiotic and collapse therapy in sanatorium may have an important part to play, is in striking contrast to that of the various manifestations of primary tuberculosis and hence must be carefully differentiated from the latter. The differential diagnosis is fully outlined. Prolonged sanatorium treatment of simple primary lesions is apparently regarded as unnecessary, and good expert supervision, with bed rest while they are ill, can keep the patients out of hospital without undue risk. This is a very significant observation and it is of interest, too, that a series of patients prematurely discharged fared no worse than the series who had an adequate course.

A rational explanation of the pathogenesis of chronic pulmonary tuberculosis, based on the study of primary tuberculous disease and chronic pulmonary tuberculosis in childhood, is given by the authors, and they present a convincing case to show that further studies on these lines is likely to contribute to a more accurate knowledge of the life history of tuberculosis in general.

There are a few minor criticisms. The X-ray illustrations, which might, with advantage, have been in closer association with the text, (positive prints throughout) are on the whole good, but, for example, in the legend Fig. 6A it is stated that there is an " area of collapse in the left lower zone (probably lingula) and possible enlargement of the left hilar glands." Surely a lateral picture, which is not shown, should have made it possible to be more definite, thus avoiding vague terms like " probable " and " possible "? The absence of any index in a book of this kind is a striking omission which should be rectified in a future edition. These criticisms apart, this study, clearly and admirably presented, and based on the wide experience of the authors should be read by all interested in tuberculosis and its varied manifestations in childhood.

PHILIP ELLMAN.

A Synopsis of Children's Diseases. By JOHN RENDLE-SHORT. London: Simpkin Marshall Ltd.; Bristol: John Wright and Sons Ltd. 1954. Pp. 620. Illus.

The purpose of this new addition to the " synopsis " Series is to provide easy reference and rapid revision of this important branch of medicine, par-

ticularly by examinees, House Physicians and General Practioners. The material is arranged and presented to suit this purpose and a useful appendix on drug dosage is provided. The style is of necessity terse and sometimes cryptic and misleading, due usually to failure to amplify or modify a statement that is intrinsically correct. The natural history of disease processes is lost sight of in the mass of tabulated matter and only a disjointed picture can be reconstructed through tedious cross-references.

The value of a book of this type depends largely on the accuracy of the facts presented, and from this point of view it is almost above reproach. In the section dealing with Tuberculosis, however, the criteria for reading the results of intradermal and jelly Mantoux Tests differ from those in general use according to the Ministry of Health publications on the subject; thus, the minimum induration for a positive intradermal test is given as 10 mm., whereas the Ministry of Health gives 6 mm., and the instruction is given to ignore erythema when interpreting the Jelly Test, whereas in general this is accepted as an indication of a positive reaction if a reaction to the plaster is excluded.

There seems little justification for perpetuating obsolete and relatively valueless physical signs such as Rivière's and D'Espine's signs or of old misconceptions which have long been disproved, such as that " bronchogenic tuberculosis " is rare in people with mitral stenosis. Many will disagree that the toxicity of Streptomycin and Dihydrostreptomycin is identical and with the omission of Calciferol in the treatment of tuberculous cervical adenitis.

J. H. P. JOHNSON.

Tuberculoses Oculaires et Tuberculoses Paraganglionnaires. Étude phtisiologique et applications thérapeutiques. By L. PAUFIQUE and J. BRUN. Paris: Masson et Cie. 1954. Pp. 186. Illus. 1,350 fr.

The authors point out, in their introduction to this book that ocular tuberculosis is not the concern of the ophthalmologist alone but that it concerns the general physician as well. They quite rightly indicate that the clinician makes little effort to understand disease conditions as they effect the eyes, and also that the eye specialist tends not to be sufficiently familiar with tuberculous disease as it affects the patient as a whole. There is thus a need for closer co-operation between the ophthalmologist and the general physician in the management of ocular tuberculosis, as well as of many other " medical " eye conditions.

Tuberculous disease when it affects the eyes is usually a sequel of some extra-ocular focus, most commonly in the chest. There may be actual bacterial invasion of the structures in the eye itself, or there may be manifestations which are an allergic response from a distant focus of infection.

The clinical manifestations of tuberculosis of the eyes are described in some detail with illustrative case reports. A further section of the book is devoted to tuberculous infection of lymphatic glands.

Emphasis is placed on the value of general measures, such as rest, in treatment, and other methods are also considered. In the opinion of the authors deep X-ray treatment of tuberculous glands may be combined with ultra-violet light with advantage to the patient. This is a view which will not be universally accepted. The authors also make the point that patients with ocular tuberculosis should not be allowed to come in contact with other patients who have open lesions, and they should therefore not be treated in ordinary sanatoria.

The text is well presented and the book fulfils a useful purpose. Its value as a work of reference would be greatly increased by the addition of a much more detailed index.

JAMES MAXWELL.

Technique des Tuberculino-Réactions et de la Vaccination par le B.C.G. Sous la direction des Docteurs COURCOUX, ANDRÉ MEYER, et J.-P. NICO. Paris: Masson et Cie. 1953. Pp. 15+lxi. Fifty-two Figures. Price not stated.

Manuel Pratique de Vaccination par le B.C.G. Par R. MANDE. Paris: Masson et Cie. 1953. Pp. 200. Illustrated. Price not stated.

These volumes, which are in many ways complementary, are issued by The Comité National de Défense contre la Tuberculose and by Le Centre Internationale de l'Infance respectively. The first, which is essentially an atlas, contains 15 pages of text on the technique and interpretation of tuberculin tests, all the standard forms of which are described and discussed, and of the technique of vaccination by B.C.G. The scarification and intradermal methods alone of the latter are described. The text is followed by 61 pages of photographic illustrations, some of which are in colour. All are of full-page length and all are of high quality.

There is no doubt that there is room for an up-to-date book on B.C.G. vaccination and the second publication (by R. Mande) is excellent and practical and fills this need admirably. The subject is dealt with from every angle, starting with a critical discussion of B.C.G. as an immunising agent, and the tuberculin tests and tuberculin allergy including the use of the vaccine itself as a testing agent. There are chapters on the selection of those for vaccination, on the technique of vaccination, on the follow-up of the patient, on the complications of vaccination, and on the tuberculous manifestations which may be observed in those who have been vaccinated in the ante-allergic phase of natural infection or have become infected immediately after vaccination. It is of interest to note that the von Pirquet test has at last lost favour in France and that the Mantoux and Jelly tests, the latter in young children, find most favour; and that the recommended methods of vaccination with B.C.G. are the scarification method of Nègre and Bretey in children and the intradermal method which is so largely used in this country. The text is accompanied by 41 excellent photographs, some of which are in colour. The book is written lucidly and critically. It is comprehensive and is worthy of a wide circulation. The two are a good combination and will be of great help to those who are embarking on this work. The illustrations in particular of tuberculin reactions, B.C.G. papule formation, and methods of techniques should be invaluable to nursing personnel on whom much of this work is bound to devolve.

CHARLES CAMERON.

Schichtbilder von Bronchialveränderungen bei der Lungentuberkulose. By H. BLAHA. Georg Thieme Verlag. Pp. viii+113; 86 illus. D.M. 18.

Tuberculous endobronchial disease and its relationship to diagnostic and therapeutic measures is reviewed in the light of the contemporary literature and a series of carefully reproduced tomographs are presented in this monograph which repay careful study.

Bronchography and tomography are frequently combined to produce convincing illustrations of stenosing bronchial disease, tuberculous bronchiectasis and broncho-cavernous lesions. Tomography establishes a means of following the progress of therapy in endobronchial disease which has previously been confirmed by bronchoscopy.

Der Einfluss der antibiotischen und chemotherapeutischen und chemotherapeutischen Behandlung auf das morphologische Bild der abheilenden Tuberkulose. By H. LÜCHTRATH. Georg Thieme Verlag. Pp. 104. 42 illus. 1954. D.M. 15.

This monograph reviews the history of chemotherapy of tuberculosis and discusses the influence of streptomycin, PAS, and thiosemicarbazone on tuberculous meningitis, miliary tuberculosis and caseous pneumonia. While chemotherapy aids and accelerates the normal defence mechanism of the body, by virtue of its action on the tubercle bacillus, the morphological pattern of healing remains essentially unchanged. The histology of these rapidly healing lesions is well reproduced and appears to have been carefully selected.

LEON CUDKOWICZ.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in the subsequent issues:

Recent Advances in Chemotherapy, Vol. III, *Antibiotics*. By F. C. O. Valentine and R. A. Shooter. London: J. and A. Churchill Ltd. 1954. Pp. viii+292. 7 illus. 27s. 6d.

Pneumoconiosis Abstracts. Vol. II. 1st Edn. London: Sir Isaac Pitman and Sons Ltd. 1954. 80s.

Guide to the Classification and Identification of the Actinomycetes and their Antibiotics. By Selman A. Waksman and Hubert A. Lechevalier. London: Baillière, Tindall and Cox. 1954. Pp. x+246. 38s. 6d.

Microbiology. By Ernest Gray. London: Crosby Lockwood and Son Ltd. 1954. Pp. x+175. Illus. 10s. 6d.

Brompton Hospital Reports. Vol. XXII. London: Research Department of the Hospital. 1953. Pp. ix+165. Illus. 15s.

British Medical Bulletin. Vol. X, No. 2: *Tuberculosis*. London: The British Council, 1954. Pp. 159. 15s.

Help for the Tuberculous. London: N.A.P.T. (revised edition). 1954. Pp. 68. 5s.

Hospital at Work. London: Max Parrish and Co. Ltd., for the Middlesex Hospital. 1954. Pp. 48. Illus. 3s. 6d.

Tuberculosis Index and Abstracts of Current Literature Quarterly. March 1954. Vol. 9, No. 1. N.A.P.T. 25s., per year $5.

La Pratique du Pneumothorax Thérapeutique. By J. Dumarest, P. Galy, and J. Germain, in collaboration with F. Parodi. Paris: Masson et Cie. 1954 (6th edition). Pp. 386. 18 illus. 1,500 fr.

Die Narkose: Ein Lehr- und Handbuch. By H. Killian and H. Weese. Stuttgart: Georg Thieme Verlag. 1954. Pp. 1003. 412 illus. D.M. 170.

Antibiotika-Fibel. Indikation und Anwendung der Chemotherapuetika und Antibiotika. By A. M. Walter and L. Heilmeyer. Stuttgart: Georg Thieme Verlag. 1954. Pp. viii+813. Tables and Figs. D.M. 79.

Thorakoskopische Eingriffe am Nervensystem. By E. Kux. Stuttgart: Georg Thieme Verlag. 1954. Pp. xii+130. Tables and Figs. D.M. 28.50.

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REPORTS

MINISTRY OF HEALTH

Renewed Attack against Tuberculosis—Preventive Measures

Local authorities have been asked by the Minister of Health, Mr. Iain Macleod, to intensify their preventive measures against tuberculosis.

He has sent to them and to hospital authorities a memorandum on "Prevention of Tuberculosis" which was prepared in consultation with his Standing Tuberculosis Advisory Committee and the Central Health Services Council. This states that the very slight improvement in notification rates "is in strong contrast to the dramatic improvement in mortality rates and emphasises the importance of renewed effort to bring the incidence of tuberculosis finally under control."

Deaths from respiratory tuberculosis in England and Wales last year fell by 1,424 or from 9,335 in 1952 to 7,911. The provisional figure of notifications was about 41,000, compared with nearly 42,000 in 1952.

The memorandum does not purport to suggest new methods of prevention but reviews the value of existing measures. Dealing with methods of control, it says it is felt that if as much effort is put into tracing the source of tuberculous infection as is put into finding out the origin of a typhoid outbreak or tracing the contacts of a smallpox patient, the decline in incidence would be accelerated. "The ubiquity of the tubercle bacillus may make this more difficult, but it does not make it a less necessary task," it is added.

Tracing of Contacts

Referring to the tracing of contacts, the memorandum states that it is rarely possible to trace them all, but it is believed that tracing can and should be carried further than it is now in many areas, if not in all.

Other aspects covered include the employment of the tuberculous, home conditions, use of B.C.G. vaccine, and tracing the source of infection. One of the points made regarding employment is that it is obviously far better that the infectious patient should be placed in suitable work where he would not be a danger to others, than that he should be allowed to find his own employment without precaution. It follows that he should be given every help to secure suitable employment for which he is fit.

So far as mass radiography is concerned, it is considered that there is much to be gained by its selective use for groups which show some evidence of special risk, rather than for the re-examination of large groups of employed persons. Special surveys in areas where, for some reason, it is thought that the incidence of tuberculosis is high have also proved of value, it is noted.

Stressing the importance of team work in the field of prevention, the memorandum says that no campaign which is not fully explained to, and supported by, the general practitioners of the area can succeed. "The family doctor has unique opportunities to advise patients and their families, and he is, of course, the vital discoverer of the early case," it is stated.

CANADIAN TUBERCULOSIS ASSOCIATION

THE Canadian Tuberculosis Association held its annual meeting in Saint John, N.B., in late June. The President of the Association, Dr. J. A. Vidal, and his management committee devoted much of their time during the first two days of the meeting to conferences with the Tuberculosis Directors, the Rehabilitation Officers and the Secretaries of the Christmas Seal Committees of the Provinces. These conferences proved to be both informative and stimulating. The first paper on the medical programme, which started on June 24, the third day of the meeting, dealt with a follow-up study of an outbreak of pulmonary tuberculosis in a rural community. This paper, as well as many of the papers which were presented in the two and one-half day medical session, evoked considerable discussion. The titles of some of the papers which were read were as follows: " The Pathogenesis of Tuberculosis (An Experimental Study)," by Dr. Hugh E. Burke; " Radiation Hazards in Fluoroscopy," by Dr. E. A. Petrie; " Comparison of Ultra-violet Light Killed Vole Bacillus Vaccine with BCG as Immunising Agent against Experimental Tuberculosis," by Dr. Earl English; " Eighteen Months' Experience with INH and Streptomycin in the Treatment of Tuberculosis at Charles Camsell Indian Hospital," by Dr. M. A. Matas; " Modern Trends in the Treatment of Bone and Joint Tuberculosis," by Dr. E. W. Ewart; " B.C.G. Vaccination in Newfoundland," by Dr. T. A. Knowling; and " The Problems of Rehabilitation," by Dr. J. A. Millet. A number of excellent papers referable to thoracic surgery were also read and discussed. At the same time the Secretaries of the Christmas Seal Committees, the Rehabilitation Officers and the Nurses carried on their own programmes. The meetings of the nurses included presentation of a paper by Miss Eldridge entitled " Student Programme in Tuberculosis Nursing "; a paper by Miss Ball entitled " Nursing Investigation of a Tuberculosis Epidemic "; a paper bearing the title " Tuberculosis Programme in Great Britain," by Miss MacLennon and Miss Connor; and papers on rehabilitation by the Hon. Milton Gregg, V.C., Minister of Labour, Canada, and by Dr. C. W. Kelly, Medical Superintendent of the Jordon Memorial Hospital, The Glades, N.B.

At the business session on the evening of the Annual Dinner, Dr. G. E. Maddison of Saint John, N.B., was appointed President for the ensuing year and Dr. E. L. Ross of Winnipeg, Manitoba, was chosen to be the President-elect.

NOTES AND NOTICES

THE BRITISH TUBERCULOSIS ASSOCIATION

THE 1954 Annual General Meeting was held at Manchester College, Oxford, on the opening day of the Annual Conference from July 7 to 10.

Subjects under discussion at the Conference were:

The Five Year Follow-Up of the Medical Research Council Controlled Trial of Streptomycin in Pulmonary Tuberculosis
Rational Drug Therapy in Pulmonary Tuberculosis
Tuberculin Testing and B.C.G.
Modern Trends in Chest Tomography
The Uses of Bronchography in Pulmonary Tuberculosis
The Pathogenesis and Prognosis of Tuberculous Pleural Effusion.

Among the speakers were: Doctors Wallace Fox, J. L. Livingstone, K. Neville Irvine, Hans Christian Olsen of Bornholm; Cynthia H. Pierce and Rene J. Dubos of the Rockefeller Institute for Medical Research, New York; J. F. Galloway, H. W. O. Frew, G. Simon, J. W. Pierce, W. S. Holden, Professor James J. Waring of the University of Colorado, and Mr. Oswald S. Tubbs.

THE THORACIC SOCIETY

THE programme for the Annual General Meeting was held on Friday and Saturday, July 16 and 17, 1954, in the Clinical Sciences Building, Manchester, is as follows:

There are to be discussions on " Cooling," with Dr. O. G. Edholm, Dr. E. J. Delorme and Dr. B. G. B. Lucas as the opening speakers.

Communications on " Byssinosis," by Dr. Schilling and Dr. Hughes and " The Intra-thoracic Manifestations of Hodgkin's Disease and the Reticuloses," by Dr. Easson.

There were also a series of short communications:

1. " The Treatment of Sarcoidosis with Streptomycin and Cortisone," by Dr. Clifford Hoyle.
2. " Liver Biopsy in Sarcoidosis and Tuberculosis," by Dr. G. Mather.
3. " The Indications for and Results in the Surgical Treatment of 30 Cases of Funnel Chest," by Mr. E. F. Chin.
4. " Œsophagitis," by Miss K. V. Lodge.
5. " The Ventilatory Response to Exercise," by Dr. F. J. Prime.

N.A.P.T.

The Fourth Commonwealth Health and Tuberculosis Conference took place at the Royal Festival Hall, London, from June 21 to June 25, 1955. Lectures, Discussions and Clinical Meetings, as well as Practical Demonstrations and visits to Sanatoria, Hospitals and Clinics, were among the main features of the Conference.

N.A.P.T.—SCOTTISH BRANCH

A REFRESHER Course on Tuberculosis is being held at the University of Glasgow from September 14 to 17. It is being arranged for doctors, nurses, health visitors, social workers and administrative officials. Subjects under discussion are:

Organisation of an Anti-Tuberculosis Campaign
Social Implications of Tuberculosis
Problems of Domiciliary Nurses in Rural Areas
Tuberculosis with Special Reference to Chemotherapy, Surgery, Preventive Aspects and the training of Nurses.

From the purely medical side:

Tuberculous Meningitis
Drug Resistance in Pulmonary Tuberculosis
Surgery in Tuberculosis
Tuberculosis and Pregnancy
Tuberculosis of the Skin, Eye and Renal Tuberculosis are being discussed.

A distinguished group of Physicians, Medical Officers of Health and Surgeons from Scotland and this country are participating in the programme, details of which are obtainable from the National Association for the Prevention of Tuberculosis.